Effect of Transcranial direct current stimulation on sensory integration and risk of falling in diabetic polyneuropathy

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Abstract

Diabetic peripheral neuropathy (DPN), presents in up to half of the people with diabetes, leading to sensory motor and autonomic impairment, and possibly increasing the risk of falling. Transcranial direct current stimulation (tDCS) modulates cortical excitability of the stimulated somatosensory cortex which in turn modifies brain functions resulting in neuroplastic changes.To investigate effect of (tDCS) on sensory integration and risk of falling in patients with diabetic polyneuropathy.Thirty patients diagnosed with diabetic polyneuropathy were enrolled in this study. They were divided randomly into two equal groups. Control group (GI) treated with designed physiotherapy program and study group (GII) treated with the same physiotherapy program plus tDCS over the somatosensory area of the left side. Treatment was conducted Three times per week for two months. Biodex balance system was used to assess sensory integration (sway index) in four sensory conditions and risk of falling pre and post treatment for both groups.Significant reductions of sway indices in all four sensory conditions and risk of fall index were observed in both groups post treatment with more reduction in favor to study group (P<0.05).Adding transcranial direct current stimulation to designed physiotherapy program result in more improvement of sensory integration and reduction of risk of falling than physical therapy alone in patients with diabetic polyneuropathy.

Key-words: *Diabetic polyneuropathy, Transcranial direct current stimulation, Biodex balance system, Sensory integration, Risk of falling.*

I. Introduction:

Diabetic polyneuropathy (DPN) is the presence of peripheral nerve dysfunction in diabetic patients [1]. It is diagnosed in 20-50% of the diabetic population [2].Peripheral neuropathies start with reduced sensitivity followed by motor nerve impairment [3].Sensory disruption leads to loss of vibration, pressure, temperature, pain and decreased

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proprioception [4]. Patients experience muscle weakness and decreased balance which affect gait control [5]. All these risk factors limit walking and other activities and increase the incidence of falling injuries [6]

Balance controlinvolves integration of sensory information from different sensory systems(eg: somatosensory, vestibular andvisual systems) that is normally interacted to maintain body's postural control. When information from one sensory system is disturbed, the central integration process depends on other systems and selects a specific response strategy to maintain postural control and so prevent falls. In patients with diabetic polyneuropathy , sensory integration can be improved via designed training. Training can performed either by corrupting the somatosensory input sensor (eg: soft surfaces) or delimiting thevisual input (eg: patching the eyes of the patient [7].

Biodex balance system used for both assessment and treatment. It providesfast and accurate evaluation of proprioceptive neuromuscular mechanisms which appear to affect both static and dynamic balance. It quantifies the ability of a person to maintain dynamic posture stability on a stable or unstable surface. It can objectively evaluate sensory integration process and predict the risk of falling in DPN patient's[8]

Transcranial direct current stimulation is non-invasive brain stimulation which modifies cortical excitability using low-amplitude direct current. [9]. It causes modulation of the cortical response to peripheral stimulation in the regions that is linked to somatosensory integration. Anodal stimulation increases the excitability of stimulated region which is responsible for effects of tDCS on somatosensory perception [10] .

Transcranial direct current stimulation on somatosensory cortex was used to improve sensory perception in heathy adults [12], older persons [13] and young adults [14]. However, To the best of our knowledge, no study showed its effect in diabetic polyneuropathy patients so the aim of our randomized controlled trial was to determine the effect of (tDCS) on sensory integration and risk of falling in patients with diabetic polyneuropathy.

II. Materials and Methods:

This randomized controlled trial was conducted at outpatient clinic of Faculty of physical therapy, Modern university for Technology and Information from May 2019 to January 2020. Ethical committee of faculty of physical therapy and institutional review board for human subject researches at Cairo University, Egypt approved the study NO:P.T.REC/012/002000. The study protocols was explained in details for each patient and inform written consent for participants in the study has been obtained up on enrolment. This study was registered with http://prsinfo.clinicaltrials.gov/prs-users-guide.html number CT04516200.

Subjects:

Thirty diabetic polyneuropathy patients with type II diabetes participated in the study. They were recruited from outpatient clinic at Faculty of physical therapy, Modern university for Technology and Information. They were diagnosed and referred from a neurologist and the diagnosis was confirmed by nerve conduction study. Patients with age ranged from (50 to 65) years , body mass index (BMI) ranged from 25-29.9 kg/m², average duration of illness of ten years and moderate severity of neuropathy ranged from9 to 11 according to Toronto clinical neuropathy scale were included in the study . Patients with diabetic ulcer and amputation ,osteoporosis, fractures of lower limbs, peripheral vascular diseases, balance disturbance due to other cause rather than diabetic peripheral neuropathy (eg: ear problems, labrynthinitis, stroke or cerebellar problems ,…etc) visual disturbance, and patients with implanted devices for pain control (eg: deep brain stimulator) were excluded from the study.

Randomization

A total of fifty diabetic patients were examined for eligibility. Twenty patients were excluded (fifteen patients didn't meet the inclusion criteria and five patients declined to participate in the study). Thirty patients were divided randomly into two equal groups; control group(G I) treated by designed physiotherapy program and study group (GII) treated with the same physiotherapy program plus tDCS over the somatosensory area of the left side **(figure 1).**Randomization process was performed by self-selecting card corresponding to one of the two groups. Subjects and examiners were blinded during randomization except for the person who organized the groups' cards.

Intervention:

The treatment was conducted three times per week for two months for both groups. Each session time was approximately 60 minutes. Patients in (GI) received designed physiotherapy program consisted of sensory integration and balance training plus sensory re-education exercise designed according to American Society of Neurorehabilitation [7].

Sensory integration and balance training are group of exercises aimed to improve feet sensation and balance. Three types of exercises were performed to patients. First exercises involved self-destabilization of the center-of-body mass in which patient was asked to exert the appropriate motor response for both static and dynamic challenges (eg, shifting their body weight to tips of the toes and to heels as in get to stand from sitting on stool; alternating stand on the right leg then the left leg stand with step forward or lateral direction). These tasks mainly concerned feed forward postural control.

Secondexercises compromised tasks whichcaused exo-destabilization of the center-of-body mass in which patient was asked to preserve balance up on standing on different consistency of the surface (foam**,** movable balance board…etc) while the therapist was pushing the patient in forward and backward directions in order to disturb patients stability. These tasks mainly concerned feedback posturalcontrol.

Thirdexercises focused coordination between leg and arm movements during walking over obstaclesand other destabilizing activities such as walking between parallel bar, walking out of parallel bar and tandem walking.

Sensory re-education exercises use different textured materials ranged from soft to rough to re-educate the nerve endings. The unaffected area was stroked with silk and the patient remembered the feelings of the stimuli then the affected area was stroked with the same material and patient was asked to try to recall the normal feelings on the affected area. The process was repeated with progression to another material.

- Patients in (GII) received the same physiotherapy program in addition to transcranial direct current stimulation over left somatosensory cortex. Transcranial direct current stimulation was conducted using (Apex Type A LLC.5 Transcranial direct current stimulator) . It consists of battery-powered device that sends constant low direct current through two electrodes attached to scalp. Each patient was asked to relax as much as possible in a comfortable sitting position. Electrode sites on the scalp were thoroughly cleaned with special substance (Nuprep). The anode electrode was placed over the primary somatosensory cortex on the left side [15]whilethe cathode electrode was placed on the supra-orbital region of the contralateral side and elastic or rubber head straps were placed around the head circumference to fix electrode in place.Primary somatosensory cortex area was determined by measuring the half distance between the vertex (CZ) and the T3 by marking 10% of the distance between the two pre-auricular points from left side according to 10-20 international system of electroencephalography electrodes placement [16]. The settings were adjusted on the tDCS stimulator to 1mA intensity and 20 min duration. The direct current initially increased in a ramp-like fashion for several seconds until reaching 1mA to avoid dizziness or vertigo, brief retinal phosphenes that may occur with sudden increase or decrease in current.

III. Outcome measurements:

Sway index and risk of fall index:

Sensory integration and risk of falling were measured using Biodex Balance System SD (Model 945-302, software version 3.12, New York). The system equipped with a circular platform which tilts twenty degrees in all directions from the horizontal plane. Biodex system controls the extent of the platform instability. The surface instability can be adjusted from very unstable (level 1) to minimal unstable (level 12). Level 6 was selected to assess balance for all patients. Patient stood on platform and was tried to maintain the center of mass within the middle of a concentric circle that showed on the systems screen.

Sensory integration test measures ability ofpatient to integrate various senses with respect to balance and ability to compensate when one or more of those senses were compromised. The modified clinical test of sensory integration and balance (M-ctsib) consisted of four conditions; *Condition one:* The patient stood on a firm surface with opened eyes and looked at a target on the display screen during platform tilt so incorporated visual, vestibular and somatosensory inputs. *Condition two:* The patient stood on a firm surface with closed eyes eliminated visual input to evaluate vestibular and somatosensory inputs during platform tilt. *Condition three:* The patient stood on a foam surface with opened eyes looked at a target on the display screen during platform tilt to evaluate somatosensory interaction with visually input.*Condition four:* The patient stood on a foam surface with closed eyes during platform tilt to evaluate somatosensory interaction with vestibular input. The device records the actual postural sway and calculates the variance from the center that is expressed as a balance index. The sway indexis the standard deviation of the stability index. The higher sway index, the more unsteady the person was during the test [17]. The patient performed three trials, trial duration was of 20s with rest period of 25s.

In ***the risk of falling test,*** the patient stood on the platform and tried to compensate for platform tilting till the end of the test trial. The test consists of three trials. The time of each trial is 20 seconds. The test calculated velocity of postural sway to predict the risk of falling. Velocity means speed of an individual's sway when trying to maintain balance.

After completion of the test, the instrument recorded the fall index and compared it to normate the data matched to same age . A highersway velocity indicates postural control deficits. Assessment of sway index for sensory integration and risk of fall index for each patient in both groups were performed pre and post treatment.

Statistical analysis used:

The measured data was collected and statistically analysed by the statistical package for social sciences (SPSS) version 22 for windows (IBM SPSS, Chicago, IL, USA).

Descriptive statistics (Mean and standard deviation) were used to measure central tendency and dispersion respectively. Un paired t-test used to compare general characteristics between both groups. Shapiro–Wilk test and Levene's test wereused to check data normality and homogeneity respectively between groups. Mixed MANOVA was performed to compare within and between groups effects on sway indices and risk of fall index. Post-hoc tests using Bonferroni correction were carried out for subsequent multiple comparison. $P < 0.05$ was considered significant.

IV. Results:

Comparison between both groups revealed no significant difference between both groups regarding the mean values of age, weight, height, BMI and duration of illness. ($P > 0.05$). Table (1)

Both groups showed significant decrease in sway indices in all conditions of sensory integration test and significant decrease in risk of fall index aftertreatment compared with that before treatment ($P > 0.001$). Table (2)

Comparison between both groups revealedno significance pre-treatment ($P > 0.05$). While post treatment there were significant reductions of sway indices in all four sensory conditions and risk of fall index in both groups post treatment with more reduction in study group ($P > 0.001$).

Table 1. Comparison of subject characteristics between the study and control groups:

	Mean ±SD		MD	t- value	p-value
	Study group	Control group			
Age (years)	57.93 ± 5.88	57.33 ± 5.09	0.6	0.29	0.76
Weight (kg)	76.26 ± 3.51	74.8 ± 3.98	1.46	1.06	0.29
Height (cm)	164.86 ± 4.25	163.13 ± 2.69	1.73	1.33	0.19
BMI (kg/m²)	28.07± 1.22	28.1 ± 1.36	-0.03	-0.07	0.94
Duration of illness (years)	10.2 ± 1.42	9.86 ± 1.68	0.34	0.58	0.56

SD, Standard deviation; MD, Mean difference; p value, Probability value

Table 2. Mean sway index and risk of fall index pre and post treatment of the study and control groups:

	Study group	Control group		
	Mean ±SD	Mean ±SD	MD (95% CI)	p value
Sway index				
Condition I				
Pre treatment	1.98 ± 0.15	2.02 ± 0.11	-0.04 (-0.14: 0.05)	0.39
Post treatment	1.06 ± 0.15	1.73 ± 0.2	-0.67 (-0.8: -0.52)	0.001
MD (95% CI)	0.92 (0.8: 1.03)	0.29 (0.18: 0.41)		
	p = 0.001	***p = 0.001***		
Condition II				
Pre treatment	2.43 ± 0.12	2.46 ± 0.11	-0.03 (-0.12: 0.05)	0.48

Post treatment	1.31 ± 0.07	2.06 ± 0.13	-0.75 (-0.83: -0.66)	0.001
MD (95% CI)	1.12 (1.04: 1.18)	0.4 (0.32: 0.46)		
	p = 0.001	***p = 0.001***		
Condition III				
Pre treatment	2.64 ± 0.19	2.67 ± 0.16	-0.03 (-0.16: 0.1)	0.7
Post treatment	1.41 ± 0.13	2.18 ± 0.14	-0.77 (-0.87: -0.66)	0.001
MD (95% CI)	1.23 (1.14: 1.32)	0.49 (0.39: 0.58)		
	p = 0.001	***p = 0.001***		
Condition IV				
Pre treatment	4.73 ± 0.14	4.75 ± 0.13	-0.02 (-0.12: 0.08)	0.65
Post treatment	3.37 ± 0.34	4.07 ± 0.32	-0.7 (-0.94: -0.44)	0.001
MD (95% CI)	1.36 (1.16: 1.53)	0.68 (0.49: 0.86)		
	p = 0.001	***p = 0.001***		
Risk of fall index				
Pre treatment	3.56 ± 0.51	3.67 ± 0.33	-0.11 (-0.43: 0.21)	0.5
Post treatment	1.89 ± 0.6	3.24 ± 0.3	-1.35 (-1.7: -1)	0.001
MD (95% CI)	1.67 (1.48: 1.86)	0.43 (0.23: 0.61)		
	p = 0.001	***p = 0.001***		

SD, Standard deviation; MD, Mean difference; CI, Confidence interval; p-value, Level of significance

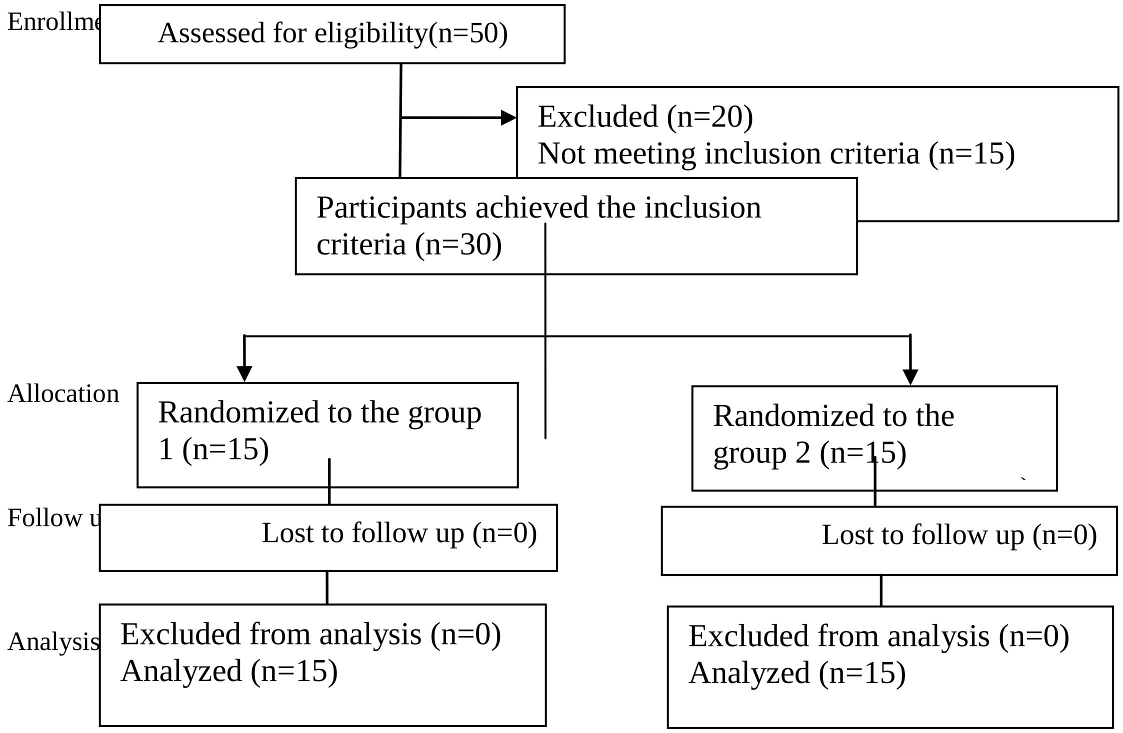

Figure 1. Flow chart of the participants during the trial.

V. Discussion:

This study was conducted to determine the influence of transcranial direct current stimulation on sensory integration and risk of falling in patients with diabetic polyneuropathy. The results showed that there were significant reductions of sway indices in all four sensory conditions and risk of fall index in both groups post treatment with more reduction in study group ($P<0.05$).

The results of this study revealed reduction of sway index in all four conditions of sensory integration test in both groups of treatment with more reduction in study group (GII). Improvement in control group (GI) may be attributed to the physiological effect of the physiotherapy program. Sensory re-education exercises retrain neural pathways and responses to stimuli to restore sensory perception of the patient [18]. It increases the sensory input to stimulate the nerve and causes neural plasticity by training the previous unused neural connections to take over for damaged pathways. Also exercises were proved to increase the proprioceptive stimulation, promote better organization and integration of sensory inputs at different CNS levels. Adequate sensorimotor processing allows adaptation to external perturbations and correct programming errors in the intended movement direction, force, and execution thus promote proper neuromuscular response, and also possible optimization of motor adjustment mechanisms this agrees with **(Fayz et al., 2020)**

The better improvement in study group (GII) may be attributed to the addition of transcranial direct current stimulation into the physiotherapy program. Diabetic polyneuropathy causes structural and functional reorganization of somatosensory cortex resulting in decreased somatosensory cortical gray matter volume to compensate the peripheral sensory neuropathy [19].Diabetes type 2 also increases GABAergic inhibitory neurotransmitter and consequently increases somatosensory cortex inhibition [20]. Anodal transcranial direct current stimulation current increases excitability of somatosensory cortex and promote long term potentiation [21].Also, anodal transcranial stinulation anodal tDCS decreases in GABA concentration resulting in decreasing its inhibitory action on the somatosensory cortex[22].This lead to improvement of sensory integration in diabetic polyneuropathy. This agrees with **(Thiago et al., 2015, Wang et al., 2015, Junhong et al., 2018 and Toni et al., 2019).**

The results of our study contradicted with the study of **(Vaseghi et al., 2014)** who showed that there is no significant effect of anodal tDCS applied to the primary sensory cortex on sensory perception. The discrepancy between the two studies may be due to adding of physiotherapy program in our study. [23]

The results of this study revealed reduction of risk of fall index in both groups with more reduction in study group (GII). Improvement in control group (GI) may be due to the physiological influence of the physiotherapy program. Balance training enhances somatosensory integration by remaining inputs within the central nervous system [24]. It also increases proprioceptive firing from the cutaneous receptors from the feet and from mechanoreceptors of the muscles during co-contraction that is produced by the swaying movement [25]. The muscle co-contraction improves motor learning which consequently enhances balance. This agree with **(Chiranjeevi et al., 2017 and Irshad et al., 2017).**

The better improvement in study group (GII) may be attributed to the addition of transcranial direct current stimulation to the physiotherapy program. Peripheral neuropathy causes balance problems via damage to sensory nerves that leads to problems in feeling any sensory changes and problems determining joint position leading to coordination difficulties [26].So, the physiological mechanism of transcranial direct current stimulation to improve balance depends on its previous mentioned effects on sensory perception. Peripheral neuropathy causes defective intracortical inhibition [27] so anodal transcranial direct current stimulation decreases neuropathic pain by increasing cortical exitability [28]. Improvements of sensory perception and pain relief enhance balance and so decrease the risk of falling in diabetic polyneuropathy. This agrees with **(Yeon et al., 2012, Diego et al., 2014 and Craig et al., 2017)**

The results of present study contradicted with the study of **(Elisabeth et al., 2017)** who showed no significant effect of anodal tDCS on risk of falling and balance. The discrepancy between the two studies may be attributed to the absence of the physical therapy intervention of their study[29].

VI. Conclusion:

Adding transcranial direct current stimulation to designed physiotherapy program result in more improvement of sensory integration and reduction of risk of falling than physical therapy alone in patients with diabetic polyneuropathy.

Disclosure statement:

There isn't any financial avail in this research

. **Conflict of interest:**

The author declares no conflict of interest.

References Conflict of interest

None.

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