



ผลของการกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกศีรษะ ต่อสมรรถภาพทางกายในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง: การศึกษานำร่องแบบสุ่มและมีกลุ่มควบคุม

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Effect of Transcranial Direct Current Stimulation on Functional Fitness in Patients with Chronic Obstructive Pulmonary Disease: A Randomized Control Pilot Study

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บทคัดย่อ

ภูมิหลังและวัตถุประสงค์: การกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกศีรษะ (tDCS) สามารถเพิ่มสมรรถภาพทางกายได้ในผู้สูงอายุที่มีสุขภาพดีและผู้สูงอายุ อย่างไรก็ตาม การศึกษาเกี่ยวกับการกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกศีรษะในโรคปอดอุดกั้นเรื้อรังยังมีจำกัด ดังนั้นการศึกษานี้มีวัตถุประสงค์เพื่อศึกษาผลของการกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกศีรษะต่อสมรรถภาพทางกายเชิงหน้าที่ในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง

วิธีการศึกษา: การศึกษานี้เป็นการทดลองแบบสุ่ม ปกปิดสองทาง และมีกลุ่มควบคุมแบบหลอก ผู้เข้าร่วมได้รับการกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกศีรษะแบบปล่อยกระแสไฟฟ้า (active tDCS) หรือแบบหลอก (sham tDCS) บริเวณ primary motor cortex เป็นเวลา 20 นาทีต่อวัน ติดต่อกัน 5 วัน ตัวแปรประเมินสมรรถภาพทางกายเชิงหน้าที่ ได้แก่ การทดสอบการยืนขาเดียว การทดสอบลุกเดินไปกลับ การทดสอบโดยการลุกนั่ง 5 ครั้ง การทดสอบความเร็วในการเดิน 4 เมตร และการทดสอบความแข็งแรงของแรงบีบมือ ถูกประเมินก่อนการกระตุ้น หลังการกระตุ้น และในระยะติดตามผลเมื่อครบ 1 สัปดาห์

ผลการศึกษา: เมื่อเปรียบเทียบกับกลุ่ม sham tDCS พบว่ากลุ่มที่ได้รับ active tDCS มีการเปลี่ยนแปลงที่ดีขึ้นอย่างมีนัยสำคัญในการทดสอบการยืนขาเดียว การทดสอบความแข็งแรงของกล้ามเนื้อขาโดยการลุกนั่ง 5 ครั้ง และการทดสอบความแข็งแรงของแรงบีบมือของมือข้างขวา หลังการกระตุ้น ($p < 0.05$) โดยผลของการเพิ่มความแข็งแรงของกล้ามเนื้อขายังคงอยู่ในระยะติดตามผล นอกจากนี้ความเร็วในการเดินที่ประเมินด้วยการทดสอบความเร็วในการเดิน 4 เมตร เพิ่มขึ้นอย่างมีนัยสำคัญในกลุ่ม active tDCS ($p < 0.05$) อย่างไรก็ตาม ผลการทดสอบลุกเดินไปกลับ ไม่พบการเปลี่ยนแปลงอย่างมีนัยสำคัญทางสถิติภายหลังการกระตุ้น เมื่อเปรียบเทียบกับภายในกลุ่มและระหว่างกลุ่ม ($p > 0.05$)

สรุป: การกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกศีรษะแบบหลายครั้งบริเวณ primary motor cortex ช่วยเพิ่มสมรรถภาพทางกายเชิงหน้าที่ โดยเฉพาะด้านการทรงตัว ความแข็งแรงของกล้ามเนื้อส่วนล่าง และความเร็วในการเดินในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง

คำสำคัญ: โรคปอดอุดกั้น, การกระตุ้นด้วยไฟฟ้ากระแสตรงผ่านกะโหลกศีรษะ, สมรรถภาพทางกาย

Abstract

Background and objective: Transcranial direct current stimulation (tDCS) has been shown to increase physical performance in both healthy adults and older individuals. However, research on tDCS in COPD is limited. Therefore, the objective of this study was to investigate the effects of tDCS on functional fitness in patients with COPD.

Methods: A randomized, double-blind, sham-controlled trial was conducted. Participants received either active or sham tDCS applied over the primary motor cortex for 20 minutes daily for five consecutive days. Functional fitness outcomes including Single-Leg Stance (SLS), Time Up and GO test (TUG), Five-Times Sit-to-Stand tests (FTSST), 4-meter gait speed test (4MGS), and hand-grip strength (HGS) were assessed at baseline, post-treatment, and at 1-week follow-up.

Results: Compared with the sham group, the active tDCS group demonstrated significantly greater improvements in the SLS, FTSST, and HGS of right hand at post-treatment ($p < 0.05$). Improvement in the FTSST was maintained at follow-up. 4MGS also improved in the active tDCS group ($p < 0.05$). However, the TUG did not demonstrate statistically significant changes following the intervention in either within-group or between-group analyses ($p > 0.05$).

Conclusion: Multi-session tDCS applied over the primary motor cortex enhanced functional fitness, particularly balance, lower-limb functional strength, and gait speed in patients with COPD.

Keywords: obstructive lung disease, transcranial direct current stimulation, physical performance

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation and oxidative stress that lead to chronic bronchitis and emphysema, resulting in structural and functional alterations of the lung, including airflow limitation, pulmonary hyperinflation, and dyspnea [1]. Furthermore, systemic inflammation and oxidative stress are associated with the ubiquitin-proteasome pathway and caspase-3 activation that lead to muscle atrophy in patients with COPD [2]. Alterations in muscle fiber composition and muscle atrophy contribute to reductions in muscle strength and endurance in patients with COPD, constituting important components of skeletal muscle dysfunction [3]. Skeletal muscle dysfunction is a critical systemic manifestation in COPD that contributes to impaired functional fitness [4]. Various domains of functional fitness including muscle strength, muscle endurance, agility, balance, and gait speed, have been reported to decline in patients with COPD [4–7].

Furthermore, brain structure and function are altered by hypoxia and chronic inflammation, leading to neuronal damage in patients with COPD [8]. Interestingly, peripheral muscle weakness is associated with alterations of the central nervous system in patients with COPD [9]. Specifically, hypoexcitability of the corticospinal pathway has been linked to reduce muscle activity in this population [9]. Given the role of corticospinal hypoexcitability in muscle weakness, transcranial direct current stimulation (tDCS) may provide a novel therapeutic approach by modulating cortical excitability to enhance functional fitness in COPD patients [9–11].

Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique that adjusts resting membrane potential depending on the polarity of the applied electrode (anodal or cathodal) [12]. A previous study demonstrated that 10 minutes of anodal tDCS applied to the motor cortex over the leg area increased the excitability of the corticospinal tract to the tibialis anterior muscle [13]. In 2020, Rostami and colleagues reported that 20 minutes of

anodal tDCS applied daily for five days to the primary motor cortex (M1) improved lower extremity functional performance in older adults [14]. Similarly, other studies have found that anodal tDCS enhances walking speed, muscle strength, and balance in patients with multiple sclerosis and in older adults [15,16]. However, the effect of tDCS on functional fitness in patients with COPD remains limited. Therefore, we hypothesized that anodal tDCS would enhance central motor drive, thereby improving functional fitness in patients with COPD. The objective in this study was to investigate the effect of five-session anodal tDCS on functional fitness in patients with COPD.

Methods

Study design

This randomized, double-blind, sham-controlled trial involved the equal allocation of thirteen participants with COPD into two groups: the sham tDCS and the active tDCS groups, thereby ensuring a 1:1 balance for forced expiratory volume in the first second (FEV1)/forced vital capacity (FVC). The study lasted approximately 14 days and was divided into four distinct phases (Figure 1). The first phase was a baseline assessment of functional fitness. The second phase consisted of a five-day tDCS treatment session. After the final tDCS session, the third phase involved post-treatment assessments of the same outcome. The final phase was a follow-up assessment, performed seven days after the final tDCS session and included the same measures. All adverse events were monitored in all phases of the study. Throughout the study, participants did not receive any additional rehabilitation or exercise intervention and continued with their usual activities, allowing for the monitoring of their natural behavior and providing a more accurate representation of their daily routine.

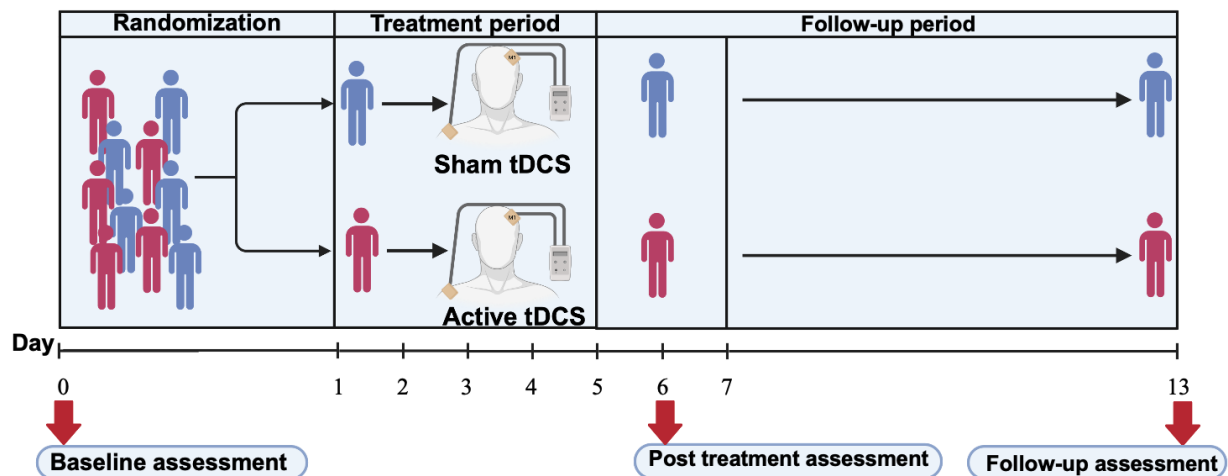


Figure 1 Timeline of study

Sample size

The sample size for this study was calculated using the formula for a randomized controlled trial to indicate a difference between two groups, based on the primary outcome (Timed Up and Go test) in older adults [14]. According to Rostami et al., the reported mean difference and pooled standard deviation yielded an estimated effect size (Cohen's d) of approximately 0.85 [14]. We provide a minimum of 80% power to identify a significant difference between groups. This calculation allowed for a type I error rate of 0.05 and considered a 20% dropout rate. Therefore, the final sample size was 13 participants for each group.

Participant recruitment and informed consent

Participants were recruited from December 2024 to February 2025 via advertisements at Nong Ruea Hospital and Phra Yuen Hospital in Khon Kaen Province, Thailand. The diagnosis of COPD was made by physicians according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [17]. Inclusion criteria were participants who met the following: (a) post-bronchodilator FEV1/FVC < 70%; (b) post-bronchodilator FEV1 30-80% of predicted value; (c) age 40-85 years old; and (d) non-regular exercise (<3 times/week and <30 min/day). Exclusion criteria were participants who met the following: (a) other respiratory diseases (such as asthma, bronchiectasis,

and pulmonary hypertension); (b) acute exacerbation within 2 months before starting studies; (c) congestive heart failure; (d) angina pectoris; (e) third-degree A-V block; (f) neuromuscular conditions (such as herniated disc and lumbar stenosis); (g) metallic implants near the electrode pacemaker; and (h) a history of neurological disorders (such as stroke and parkinson's disease). Before the commencement of the study, each participant underwent a medical history review and physical examination by a chest medicine specialist to identify any health issues. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Khon Kaen University Ethics Committee for Human Research (identifier number: HE651421). All participants provided written informed consent. This study was registered with the Thai Clinical Trials Registry (TCTR20241111001; first registered on 11 November 2024; <https://www.thai-clinicaltrials.org/show/TCTR20241111001>).

Randomization and blinding

After obtaining informed consent and completing baseline assessments, the researcher allocated a sequential identification number to each participant and provided a research assistant with participants' results of FEV1/FVC, and FEV1 % predicted. The research assistant then generated a computerized allocation schedule that balanced FEV1 % predicted among the treatment conditions. Participants were

randomized in a 1: 1 ratio to groups A or B and were instructed to continue their routine medication regimen throughout the trial. Participants were blinded to whether they received active or sham stimulation. Moreover, the assessor of outcomes was blinded to participants' clinical context and treatment allocation.

Transcranial direct current stimulation procedure

The transcranial direct current stimulation (tDCS) was applied using wet electrode pads (5 x 7 cm) connected to a battery-powered device (ProtableT-DCS, Khon Kaen, Thailand) with a maximum output of 2 mA. Anodal tDCS targeted the left primary motor cortex (M1 or C4 according to the international 10–20 EEG system), known for its role in neuronal plasticity related to motor function, following the 10-20 electrode placement system. The cathode was placed on the right shoulder. The stimulation protocol consisted of 20 minutes of tDCS, including 30 seconds of ramp-up and ramp-down periods before and after applying a 2-mA direct current, administered once daily for 5 consecutive days. The tDCS device also supported masked (sham) stimulation, where the control switch was obscured by an opaque adhesive during stimulation, masking it from participants. Additionally, the power indicator visible to participants was illuminated during both active and sham stimulations. In the sham condition, however, the current was stopped after 30 seconds.

Outcome measurement

Functional fitness in this study consists of the Single-Leg Stance test (SLS), the Time Up and Go (TUG) test, the Five-Time Sit-to-Stand Test (FTSST), the 4-meter Gait Speed test (4MGS), and the Hand Grip Strength test (HGS).

The SLS was evaluated for static balance, in which participants stood on one leg with unsupported knee flexion at 90° as long as possible with their eyes open. Time was recorded until the leg touched the floor or subsequently after 120 seconds. Finally, the

mean of three measurements was used for analysis [18].

The TUG was evaluated for dynamic balance and agility. Participants stood up from the chair and walked 3 meters, then returned to sit down as quickly as possible. Time was recorded from the moment participants stood up until they were completely seated. The mean of three-time measurements was calculated to evaluate this field study [19].

The FTSST was evaluated for lower extremity strength. Participants were instructed to cross their arms over their chest and sit in a position on an armless chair. Then, the assessor told participants to stand and sit for five repetitions as quickly as possible. The time was recorded when the assessor said “Go” and stopped at the buttocks of participants touching the seat following the fifth stand [20].

The 4MGS was evaluated for gait speed [21]. Participants were instructed to walk at a comfortable or normal pace, and their times were recorded at a 4-meter timing zone or after a 2-meter acceleration zone and before a 2-meter deceleration zone, respectively [21]. Participants were assessed during two walking conditions—a comfortable pace and a rapid pace—with each condition repeated three times [21]. The velocity was calculated by dividing distance by time, and the mean velocity of three measurements was determined to assess both usual and maximum walking speed in this study [21].

The HGS was assessed as a measure of upper limb muscle strength using a handgrip dynamometer [22]. Participants were seated in a chair with the elbow of the assessed arm flexed at 90 degrees and instructed to squeeze the dynamometer as forcefully as possible. Each hand was tested three times, and the highest value from each side was recorded [23].

Statistical analysis

All statistical analyses were performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA). This study used the Shapiro-Wilk test to assess the normality of data distribution. Baseline anthropometric

and physiological characteristics are presented as mean $\pm$ standard deviation (SD). Data of functional fitness are presented as mean $\pm$ standard error (SE). Between-group comparisons at post-treatment and follow-up were conducted using repeated-measures ANCOVA, with baseline values included as covariates to adjust for baseline differences. Within-group changes across baseline, post-treatment, and follow-up assessments were also analyzed using repeated-measures ANCOVA. Statistical significance was set at $p < 0.05$.

Results

A total of ninety patients with COPD were screened for eligibility. Sixty-four patients were excluded for the following reasons: fifty-three presented with mild COPD, two had experienced an exacerbation within the previous two months, one had congestive heart failure, and eight declined to participate. Ultimately, twenty-six patients met the inclusion criteria and provided informed consent. These participants were randomly allocated to either the sham tDCS group or active tDCS group, as shown in Figure 2.

Baseline characteristics of the two groups are summarized in Table 1. No significant differences were observed between groups in demographic or clinical parameters, including age, body mass index (BMI), blood pressure, heart rate, respiratory rate, FEV_1 , $FEV_1\%$ predicted, FVC, FVC% predicted, and FEV_1/FVC ratio, ($p > 0.05$).

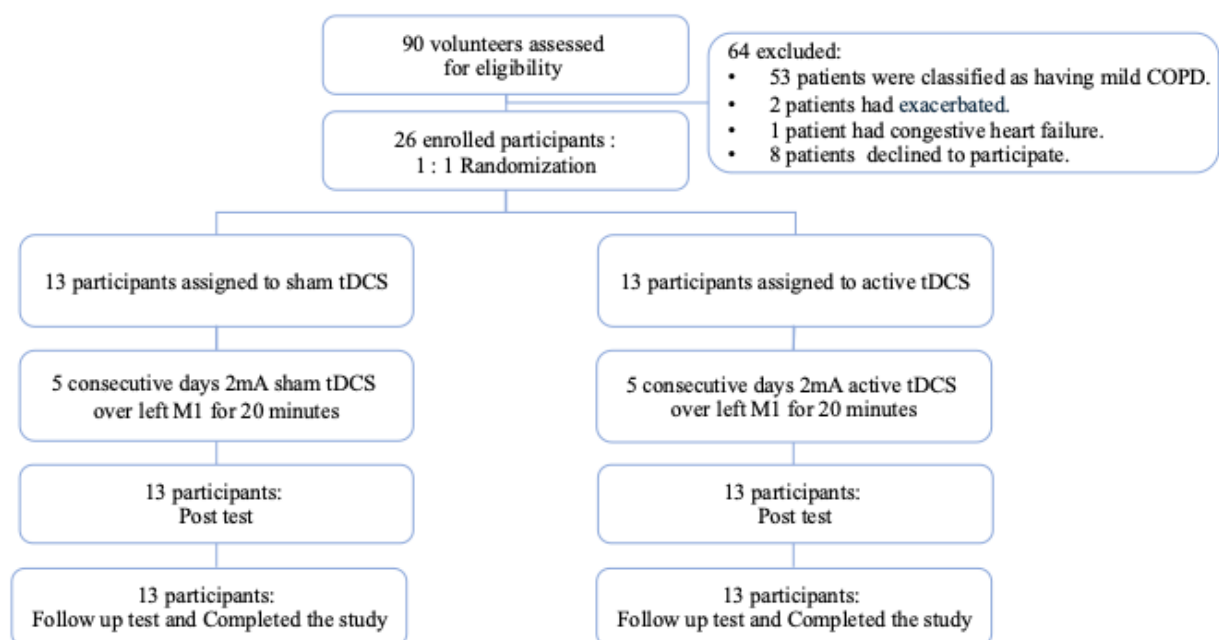


Figure 2 Flow of participants

Table 1 Baseline anthropometric and physiological characteristics of participants

	Sham tDCS (n = 13)	Active tDCS group (n = 13)	p-value
Age (yr)	67.23 ± 8.04	72.62 ± 7.51	0.09
BMI (kg/m ²)	19.91 ± 3.58	20.98 ± 4.18	0.494
RR (bpm)	19.38 ± 3.20	20.00 ± 3.65	0.652
HR (bpm)	85.46 ± 15.54	85.84 ± 7.74	0.937
SBP (mmHg)	134.92 ± 9.57	127.84 ± 21.74	0.293
DBP (mmHg)	78.00 ± 9.26	74.23 ± 12.14	0.191
FEV ₁ /FVC	50.63 ± 8.89	49.64 ± 7.40	0.760
FEV ₁ (L)	1.50 ± 0.48	1.26 ± 0.39	0.188
FEV ₁ %predicted	58.23 ± 15.96	56.30 ± 12.52	0.736
FVC (L)	2.96 ± 0.75	2.52 ± 0.62	0.124
FVC% predicted	92.54 ± 24.42	89.76 ± 14.72	0.729

Data are presented as mean ± SD. BMI, body mass index; RR, respiratory rate; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; FEV₁, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity.

Effect of tDCS on functional fitness

The SLS: Between-group comparison, the active tDCS group demonstrated greater improvement than the sham tDCS group at post-treatment ($p = 0.023$, partial $\eta^2 = 0.206$; Table 2). Specifically, the active group showed an increase in balance time, whereas the sham group remained relatively unchanged. Within-group analysis confirmed this finding, with the active group demonstrating a significant improvement from baseline to post-treatment (mean difference [MD] = +12.845 sec, $p = 0.003$; Table 3), while no significant changes were observed in the sham group.

The TUG: No significant between-group differences were observed at either post-treatment or follow-up (Table 2). Within-group analysis showed no change in the sham group, while the active group significantly reduced from baseline to post-treatment (MD = - 0.654 sec, $p = 0.017$), though this effect was not maintained at follow-up (Table 3).

The FTSST: The active tDCS group demonstrated greater improvement than the sham tDCS group at both post-treatment and follow-up ($p = 0.045$, partial $\eta^2 = 0.178$; and $p = 0.037$, partial $\eta^2 = 0.190$, respectively; Table 2). Within-group analysis showed that the sham group remained stable, whereas the active tDCS group significantly improved their performance, completing the test faster at both post-treatment (MD = -1.180 sec, $p < 0.001$) and follow-up (MD = -1.308 sec, $p < 0.001$) compared to baseline (Table 3).

The 4MGS: Regarding usual gait speed, the active tDCS group showed greater improvement than the sham group at follow-up ($p = 0.05$, partial $\eta^2 = 0.187$; Table 2), with a significant within-group increase from baseline (MD = +0.11 m/s, $p = 0.023$). For maximum gait speed, the active group outperformed the sham group at post-treatment ($p = 0.008$, partial $\eta^2 = 0.331$; Table 2). Within-group analysis highlighted a significant increase in maximum speed in the active group from baseline to post-treatment (MD = +0.144m/s, $p = 0.001$), whereas no significant changes were observed in the sham group.

The HGS: No significant between-group differences were found at either time point (Table 2). However, within groups analysis revealed a specific effect in the active tDCS group: right-hand grip strength significantly increased from baseline to post-treatment (MD = +1.729 kg, $p = 0.028$; Table 3). No significant changes were observed for the left hand or in the sham group.

Adverse events

No serious adverse events were reported. Five participants in the active tDCS group experienced mild, transient itching at the electrode site that required no medical intervention.

Table 2 Comparative analysis of outcomes between the Sham tDCS group (n = 13) and the Active tDCS group (n = 13) across identical time points, adjusted for baseline values using ANCOVA.

Outcomes	Sham tDCS		Active tDCS		Between group difference		
	Mean	SE	Mean	SE	Mean	SE	p-value
Single Leg Stance test (sec)							
Baseline	31.21	0	31.21	0	-	-	-
Post treatment	30.22	3.922	44.06	3.92	-13.82	5.66	0.023 [#]
Seven-day post treatment	30.72	4.46	39.76	4.46	-9.04	6.44	0.174
Time Up and GO test (sec)							
Baseline	7.36	0	7.36	0	-	-	-
Post treatment	7.45	0.24	6.70	0.25	0.74	0.36	0.051
Seven-day post treatment	7.28	0.26	6.92	0.28	0.36	0.39	0.370
Five Times Sit-to-Stand test (sec)							
Baseline	8.20	0	8.20	0	-	-	-
Post treatment	7.78	0.26	7.02	0.24	0.76	0.35	0.045 [#]
Seven-day post treatment	7.90	0.33	6.89	0.30	1.01	0.46	0.037 [#]
4-meter Gait Speed test (m/sec)							
Usual speed							
Baseline	1.34	0	1.34	0	-	-	-
Post treatment	1.32	0.041	1.42	0.046	-0.09	0.064	0.175
Seven-day post treatment	1.32	0.041	1.44	0.045	-0.131	0.063	0.050 [#]
Maximum speed							
Baseline	1.62	0	1.62	0	-	-	-
Post treatment	1.60	0.036	1.762	0.038	-0.158	0.053	0.008 ^{##}
Seven-day post treatment	1.633	0.058	1.742	0.061	-0.109	0.086	0.219

Data are expressed as mean $\pm$ SD. # Represents a significant difference between group ($p < 0.05$).

Represents a significant difference between group ($p < 0.01$)

Table 2 Comparative analysis of outcomes between the Sham tDCS group (n = 13) and the Active tDCS group (n = 13) across identical time points, adjusted for baseline values using ANCOVA. (Cont.)

Outcomes	Sham tDCS		Active tDCS		Between group difference		
	Mean	SE	Mean	SE	Mean	SE	p-value
Right hand							
Baseline	27.92	0	27.92	0	-	-	-
Post treatment	27.48	0.76	29.66	0.72	-2.18	1.10	0.064
Seven-day post treatment	28.34	0.76	28.92	0.72	-0.58	1.114	0.607
Left hand							
Baseline	27.11	0	27.11	0	-	-	-
Post treatment	26.10	0.935	27.94	0.935	-1.83	1.34	0.185
Seven-day post treatment	27.06	1.08	28.44	1.08	-1.38	1.54	0.380

Data are expressed as mean $\pm$ SD. # Represents a significant difference between group ($p < 0.05$).

Represents a significant difference between group ($p < 0.01$)

Table 3 The differential outcomes within the group observed at baseline, post-treatment, and follow up

Outcomes	Sham tDCS					Active tDCS					Effect size	
	Mean	SE	95% Confidence interval		p-value	Effect size	Mean	SE	95% Confidence interval			p-value
			Lower	Upper					Lower	Upper		
Single-Leg Stance test												
Baseline-Post treatment	0.981	3.922	-7.132	9.094	0.805	N/A	-12.845	3.922	-20.959	-4.732	0.003**	0.90
Baseline-Follow up	0.496	4.459	-8.728	9.719	0.805	N/A	-8.547	4.459	-17.771	0.677	0.068	N/A
Time Up and GO test												
Baseline-Post treatment	-0.088	0.239	-0.586	0.409	0.715	N/A	0.654	0.250	0.132	1.175	0.017*	0.72
Baseline-Follow up	0.080	0.262	-0.468	0.627	0.764	N/A	0.440	0.275	-0.133	1.101	0.125	N/A
Five Times Sit-to-Stand test												
Baseline-Post treatment	0.425	0.259	-0.114	0.964	0.116	N/A	1.180	0.238	0.684	1.676	<0.001***	1.38
Baseline-Follow up	0.296	0.334	-0.398	0.990	0.385	N/A	1.308	0.307	0.670	1.946	<0.001***	1.18
4-meter Gait Speed test												
Usual speed												
Baseline-Post treatment	0.008	0.041	-0.079	0.095	0.844	N/A	-0.082	0.046	-0.177	0.014	0.090	N/A
Baseline-Follow up	0.020	0.041	-0.065	0.106	0.622	N/A	-0.111	0.045	-0.205	-0.017	0.023*	0.68
Maximum speed												
Baseline-Post treatment	0.014	0.036	-0.061	0.089	0.703	N/A	-0.144	0.038	-0.224	-0.065	0.001***	1.05
Baseline-Follow up	-0.015	0.058	-0.137	0.107	0.796	N/A	-0.125	0.061	-0.253	0.003	0.056	N/A
Hand Grip Strength												
Right hand												
Baseline-Post treatment	0.452	0.761	-1.147	2.050	0.560	N/A	-1.729	0.722	-3.245	-0.212	0.028*	0.66
Baseline-Follow up	-0.409	0.767	-2.020	1.202	0.600	N/A	-0.992	0.727	-2.520	0.536	0.189	N/A
Left hand												
Baseline-Post treatment	1.012	0.935	-0.923	2.946	0.291	N/A	-0.891	0.935	-2.754	1.115	0.390	N/A
Baseline-Follow up	0.058	1.081	-2.177	2.294	0.957	N/A	-1.328	1.081	-3.563	0.908	0.232	N/A

Data are expressed as mean ± SE. * Represents a significant difference after treatment within group (p<0.05). ** Represents a significant difference after treatment within group (p<0.01). ***Represents a significant difference after treatment within group (p<0.001)

Discussion

The present study demonstrates that anodal tDCS applied to M1 at an intensity of 2 mA for 20 minutes daily over 5 consecutive days can improve functional fitness including balance, lower-limb muscle strength, and gait speed in patients with COPD.

Deterioration of functional fitness, which includes muscle strength, balance, agility, and gait speed is an important clinical issue in patients with COPD that associated with skeletal muscle dysfunction. There was a decrease in muscle strength of the quadriceps, pectoralis, and latissimus dorsi muscles. Quadriceps muscle strength was positively correlated with the cross sectional area of thigh muscles [24]. In addition, reduction of maximal voluntary quadriceps contraction (QMVC) in patients with COPD was also reported when compared with healthy subjects and the cortical silent period (CSP) of the COPD group was longer than the healthy group during the QMVC [9]. These findings suggest reduced excitability of the corticospinal pathway to skeletal muscle in patients with COPD, which led to skeletal muscle weakness [9]. Reduction of muscle strength contributes to declining agility, balance, and gait speed in patients with COPD [25–27].

According to a previous study, anodal-tDCS for 10 minutes applied to the leg area of the motor cortex can increase excitability of the corticospinal tract to the tibialis anterior muscle, as demonstrated by increased motor evoked potential (MEP) amplitude measured with TMS in healthy subjects [13] we examined whether tDCS at currents of 2 mA could effect similar changes in the excitability of deeper cortical structures that innervate muscles of the lower leg. Similar to the hand area, 10 min of stimulation with the anode over the leg area of the motor cortex increased the excitability of corticospinal tract projections to the tibialis anterior (TA). Similarly, previous study found that anodal-tDCS current intensity of 2 mA for 10 minutes on M1 decreased CSP in patients with COPD, demonstrating increased excitability of the brain to skeletal muscle via

corticospinal pathway as well [28]. In the present study, anodal tDCS improved FTSST and right HGS, suggesting increased lower and upper limb muscle strength, respectively [22,29]. Consistent with this, previous studies have reported that anodal tDCS can improve functional fitness, including lower limb muscle strength and hand grip strength in older adults and amateur badminton players [14,30]. The possible mechanism by which tDCS improves muscle strength is that anodal tDCS over motor cortex increase MEP amplitude and muscle electromyogram activity, indicating enhanced corticospinal excitability and greater motor unit recruitment, which could underlie improved motor performance [31]. These effects may be mediated, at least in part, by increased corticospinal drive leading to greater muscle strength.

This study also found that anodal tDCS improved SLS and 4MGS, suggesting enhanced balance and gait speed in patients with COPD. An increase in skeletal muscle strength contributes to increased agility, balance, and gait speed; previous studies have shown that anodal-tDCS can improve TUG, SLS, and 4MGS [32,33]. Other reports indicate benefits of anodal-tDCS on FTSST, TUG, 10MWT, functional strength of the lower limb, and static and dynamic balance [14–16]. Enhancement of corticospinal pathway excitability and motor unit recruitment contribute to increase muscle strength, which importance component for improving balance [13,32]. Improvement of muscle strength and balance influence to initiate movement and generate sufficient force to improve gait speed [34]. Hence, anodal-tDCS at 2 mA for 20 minutes may improve physical performance by increasing corticospinal excitability from the brain to skeletal muscle in patients with COPD.

Our study has several limitations. First, retention effect was assessed only up to one-week post-stimulation, limiting conclusions about the durability of effects beyond the short-term follow-up. Previous studies have recommended follow-up periods of approximately 3–6 months to more adequately

evaluate the sustainability of treatment responses [35,36]. Future research should include longer follow-up periods to assess long-term durability. Second, we did not include mechanistic measures (e.g., MEPs, intracortical inhibition, or biomarkers such as brain-derived neurotrophic factor); thus, the specific neurophysiological mechanisms underlying the improved motor performance remain speculative. Third, we did not vary stimulation dose or montage, and therefore cannot determine the optimal stimulation parameters for maximizing and prolonging benefits. Finally, the small sample size and the inclusion of participants with moderate to severe COPD limit generalizability and should be acknowledged.

Conclusion

Multi-session anodal tDCS applied to the primary motor cortex was associated with selected measures including muscle strength, balance, and gait speed in patients with moderate to severe COPD. Furthermore, improvements in lower-limb muscle strength, as indicated by the FTSST, were maintained at short-term follow-up, suggesting that tDCS may serve as a non-invasive neuromodulator adjunct to enhance rehabilitation outcomes.

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Conflict of Interest

Author(s) declared none.

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