Research paper

Effects of transcranial direct current stimulation over the supplementary motor area body weight-supported treadmill gait training in hemiparetic patients after stroke.

Atsushi Manji[a,b], Kazu Amimoto[a], Tadamitsu Matsuda[c], Yoshiaki Wada[d], Akira Inaba[e],
Sangkyun Ko[f]

a Department of Human Health Science, Tokyo Metropolitan University, 7-2-2-10 Higashi-Ogu, Arakawa-ku, Tokyo 116-0012, Japan
b Department of Rehabilitation, Saitama Misato Sogo Rehabilitation Hospital, Japan
c Department of Physical Therapy, Faculty of Health Sciences, Josai International University, Japan
d Nissan Tamagawa Hospital Rehabilitation Center, Japan
e Department of Neurology, Kanto Central Hospital, Japan
f Department of internal medicine, Saitama Misato Sogo Rehabilitation Hospital, Japan

Highlights:

- Transcranial direct current stimulation (tDCS) is used in a variety of disorders after stroke.
- We combined tDCS on supplementary motor area (SMA) with body weight-supported treadmill training and verified its effects.
- tDCS over the SMA contributes to improvement in gait ability in hemiparetic patients after stroke.

Keywords:
Stroke, Transcranial direct current stimulation, Body weight-supported treadmill training, Supplementary motor area

Abstract:

Transcranial direct current stimulation (tDCS) is used in a variety of disorders after stroke including upper limb motor dysfunctions, hemispatial neglect, aphasia, and apraxia, and its effectiveness has been demonstrated. Although gait ability is important for daily living, there were few reports of the use of tDCS to improve balance and gait ability. The supplementary motor area (SMA) was reported to play a potentially important role in balance recovery after stroke. We aimed to investigate the effect of combined therapy body weight–supported treadmill training (BWSTT) and tDCS on gait function recovery of stroke patients. Thirty stroke inpatients participated in this study. The two BWSTT periods of 1 weeks each, with real tDCS (anode: front of Cz, cathode: inion, 1 mA, 20 minutes) on SMA and sham stimulation, were randomized in a double-blind crossover design. We measured the time required for the 10-Meter Walk Test (10MWT) and Timed Up and Go (TUG) test before and after each period. We found that the real tDCS with BWSTT significantly improved gait speed (10MWT) and applicative walking ability (TUG), compared with BWSTT + sham stimulation periods ($p<0.05$). Our findings demonstrated the feasibility and efficacy of tDCS in gait training after stroke. The facilitative effects of tDCS on SMA possibly improved postural control during BWSTT. The results indicated the implications for the use of tDCS in balance and gait training rehabilitation after stroke.

1. Introduction

Noninvasive brain stimulation (NIBS) such as transcranial direct current stimulation (tDCS) is reportedly effective for the treatment of paralysis after stroke1). tDCS is used in a variety of disorders including upper limb paralysis2), hemispatial neglect3), aphasia4), and apraxia5), and its effectiveness has been demonstrated. However, there are few reports on the use of tDCS in improving balance and gait ability after stroke6)7), which are important for activities of daily living8).

Some intervention studies used tDCS to improve lower limb functions and to treat balance and gait disorders. The use of anodal tDCS on the lower leg motor area enhanced knee extension force6), postural stability, and lower extremity strength7) of stroke patients and promoted positive changes in static balance and gait velocity in children with cerebral palsy9) and patients with Parkinson disease 10). In these studies, tDCS was applied over the lower limb region of the primary motor area (M1) to examine the effects on lower limb motor function and gait ability. The M1 area in the cerebral cortex plays a role in voluntary movement of the lower limbs, and therefore, balance and gait. Meanwhile, the premotor area and supplementary motor area (SMA) play a role in planning and adjustment of gait movement11). Specifically, the SMA plays an important role in the recovery of balance and walking ability and anticipatory postural adjustment, which is important for maintaining balance during walking11).

tDCS is also reportedly effective in combination with other therapies10). Studies in post-stroke patients have combined therapy with tDCS stimulation over the upper limb region of the M1 and constraint-induced movement therapy as well as robotic training for upper limb paralysis12). tDCS stimulation over the inferior parietal gyrus has also been combined with prism adaptation therapy for hemispatial neglect13) and speech therapy for aphasia14). Robotic gait training in combination with tDCS was used and investigated as therapy to improve the walking ability of stroke patients15).

Body weight–supported treadmill training (BWSTT), a new method for treatment of gait disturbance after stroke has been also used and has been effective for improving walking speed and asymmetrical posture during walking16).

Thus, we surmised that the combined use of BWSTT and tDCS over the SMA would enhance the improvement in gait recovery after stroke. This study aimed to clarify the effects of combined therapy with tDCS and BWSTT in hemiparetic patients after stroke on improvement in walking ability.

2. Materials and methods

This is a double-blind, randomized crossover comparative study of post-stroke hemiparetic patients in a rehabilitation hospital. The inclusion criteria were new-onset supratentorial lesion and a gait disorder, ability to walk 20 m with supervision or slight assistance, and ability to undergo BWSTT. The exclusion criteria were orthopedic/systemic diseases that limit exercise therapy, severe dementia/higher brain dysfunction with difficulty understanding directions, implanted metal in the head or implanted cardiac pacemaker, and difficulty undergoing BWSTT, as judged by the physician in charge.

Of the 262 patients recruited, 224 were excluded. Of the 38 remaining subjects, 30 consented to participate. The subjects (age, 45–79 years) included 21 men and 9 women and were divided into two groups (groups A and B, n=15 in each group). Two intervention periods were set, and the pre- and post-intervention periods were determined in each group for evaluation. The interval between intervention periods was 3 days, and evaluations were carried out the day after each final intervention day. During each intervention period, real or sham tDCS stimulation was performed. In group A, tDCS (real stimulation) and BWSTT were performed during the first period, whereas sham stimulation and BWSTT were performed during the second period. In group B, the intervention was performed by switching the order of stimulation (real/sham) combined with BWSTT (Fig. 1).

In the intervention periods, tDCS was applied using a DC stimulator (NeuroConn GmBH, Ilmenau, Germany) and two saline-soaked electrodes (5×5 cm). The anode electrodes was positioned 3.5 cm anterior to Cz according to the International 10/20 EEG System17). The cathode was positioned over the inion18)19). Stimulation was performed at 1.0 mA for 20 min during BWSTT. The real/sham stimulation was set by entering a password, which prevents the subjects/persons performing the intervention from knowing the type of stimulation applied. BWSTT was performed once a day for 20 min for a period of 1 week. Subjects walked on a treadmill with 20% body weight support. The walking speed was gradually increased by setting it at 80%–90% of the subject’s maximum on the treadmill, which was determined based on the difficulty in walking continuously, self-estimation, and foot dragging. Physical assistance was avoided during BWSTT.

The 10-Meter Walk Test (10MWT) and Timed Up and Go Test (TUG) were the primary evaluation items. Measurements were performed twice and we used the average score as the representative value for the statistical analysis. The secondary evaluation items were the Fugl-Meyer Assessment of the Lower Extremity, Performance Oriented Mobility Assessment, and Trunk Impairment Scale. The differences in basic and clinical characteristics in each group were analyzed using the t-test, Mann-Whitney test, and chi-square test. Two-way repeated measures analysis of variance (ANOVA) was performed, using time required for the walk tests (10MWT and TUG) and scores of evaluation items during the pre- and post-intervention periods as dependent variables after confirming normality of variables by Shapiro-Wilk test. Groups and intervention periods were the factors used to test the presence or absence of the main effect as well as interactions among factors. When a main effect and interaction were present, a simple main effects test was performed using Bonferroni’s post hoc analysis. p Values <0.05 were considered statistically significant. Statistical analyses were carried out using SPSS statistics 23 (IBM Inc., Armonk, NY, USA).

This study was approved after ethics review by Tokyo Metropolitan University and Saitama Misato

Sogo Rehabilitation Hospital. We explained the study details to the subjects orally and in writing and they provided signed consent. We performed tDCS according to safety standards and guidelines.

3. Results

There were no differences in the basic or clinical characteristics between the groups (Table 1). The results of assessment are shown in Table 2. In the primary evaluation items, two-way repeated measures ANOVA showed main effects in the intervention period (10MWT: $F_{1.2, 34.3}=35.2$, $p<0.001$; TUG: $F_{1.3, 36.8}=26.1$, $p<0.001$) and interaction with the intervention period and groups (10MWT: $F_{1.2, 34.3}=3.2$, $p=0.046$; TUG: $F_{1.3, 36.8}=3.9$, $p=0.026$). The simple main effects test demonstrated a significant difference after real tDCS stimulation in both groups compared with the sham stimulation period ($p<.005$). Meanwhile, the secondary evaluation items, analysis of lower limb/trunk function and balance ability, showed that the main effects were associated with the intervention period ($p<0.005$). No main effect with the groups or interaction was observed.

4. Discussion

Results suggest that anodal tDCS over the SMA may enhance improvement in gait ability in combination with BWSTT in hemiparetic patients after stroke. Previous research combined robotic gait training with tDCS combination therapy for gait rehabilitation after stroke. Geroin et al.15) include 30 chronic stroke patients and found positive effects of robotic gait training compared with the usual over-ground gait training, but anodal tDCS had no additional effect on the lower leg motor area. Meanwhile, Danzl et al.20) showed that active tDCS brought greater improvement than sham stimulation, based on the results of their intervention experiment on 8 chronic stroke patients. These studies included chronic stroke patients as participants (2 years from onset). The present study included patients in an earlier stage of stroke and investigated through comparison with the BWSTT effects only. These results suggest that the efficacy of incorporation into the gait rehabilitation after stroke of the tDCS combined therapy and from earlier stage. Furthermore, previous research verified the effect of anodal tDCS on the lower leg motor area, whereas we applied anodal tDCS on the SMA.

Postural adjustments of the SMA cause anticipatory muscle activity when raising the upper limb, suppressing the movement of the trunk centroid, and allowing performance of stable actions21). As to the application of tDCS, stimulation over the SMA could modulate the anticipatory postural adjustments22). In walking, adjustments enable the hip joint to extend before forward movement during the initial stance and the centroid to shift toward the contralateral side prior to swing. Patients with Parkinson disease have deficiency in these actions and are characterized by a decrease in trunk motion during walking, leading to decreased balance activity and increased risk of falls23). Patients with stroke also present a forward movement of the trunk during the initial stance on the paralyzed side, a shift of the centroid toward the contralateral side at swing of the leg on the paralyzed side, and insufficient righting with the trunk. These lead to poor balance due to compensatory trunk flexion toward the contralateral side24).

Although BWSTT should improve standing/walking by reducing balance-related load, trunk movement is likely to remain more prominent than in healthy individuals, thus inhibiting the ability to step effectively. This condition may interfere with improvement in gait ability by BWSTT.

The SMA is important for controlling balance in hemiparetic patients after stroke and is also associated with improvement in balance ability during rehabilitation25). Our study suggests that anodal tDCS enhanced SMA activity to improve balance by decreasing trunk movement caused by stepping and a shift of the centroid to match the moving treadmill speed. This may have enhanced the effect of BWSTT on gait and contributed to recovery of balance ability.

In a previously reported study, stimulation of the M1 resulted in improvement in gait ability26). A possible mechanism is an increase in voluntary movement of the lower limbs. Owing to the mechanical characteristics of tDCS (application to a wide area), stimulation of the M1, which lies between electrodes, may be input to facilitate lower limb activity during walking, which supports improvement in training effects. A control study using different electrode positions, analysis of trunk movement during walking, and examination of effects on standing/walking balance using kinetic/kinematic and motion analysis as well as analysis of the movement of the centroid is necessary.

The secondary evaluation items, including lower limb function, trunk function, balance ability, and activities of daily living, showed no significant improvement with real tDCS stimulation. This is presumably because the intervention period was short and the sensitivity was lower, compared to results obtained when time was used as a variable in the assessment of primary evaluation items. Another possibility is the electric stimulation to the SMA during walking; thus, it may be thought that the effect was specific to walking.

In future studies, the intervention period needs to be extended and details of each evaluation item need to be analyzed.

The limitations of the study include its crossover design and undefined follow-up period. Thus, the long-term effects of real tDCS stimulation on improvement in gait ability remain unclear. In addition, the study did not analyze the effects on independence in activities of daily living or the risk of falls. Extension of the intervention period, adequate follow-up, and validation using a randomized controlled trial are also necessary. The indications for tDCS to improve gait, reduce paralysis, and promote independent walking should be analyzed, and the application and details need to be studied.

5. Conclusions

Our study suggests that therapy with tDCS over the SMA combined with BWSTT contributes to an improvement in gait ability in hemiparetic patients after stroke. This can be used as a new approach to gait rehabilitation in these patients.

References

1) Marquez J, van Vliet P, McElduff P, et al. Transcranial direct current stimulation (tDCS): does it have merit in stroke rehabilitation? A systematic review. Int J Stroke. 2015; 10(3): 306–16.

2) Bastani A, Jaberzadeh S. Does anodal transcranial direct current stimulation enhance excitability of the motor cortex and motor function in healthy individuals and subjects with stroke: a systematic review and meta-analysis. Clin Neurophysiol. 2012; 123(4): 644–57.

3) Jacquin-Courtois S. Hemi-spatial neglect rehabilitation using non-invasive brain stimulation: or how to modulate the disconnection syndrome? Ann Phys Rehabil Med. 2015; 58(4): 251–8.

4) ALHarbi MF, Armijo-Olivo S, Kim ES. Transcranial direct current stimulation (tDCS) to improve naming ability in post-stroke aphasia: a critical review. Behav Brain Res. 2017; 29; 332: 7–15.

5) Bolognini N, Convento S, Banco E, et al. Improving ideomotor limb apraxia by electrical stimulation of the left posterior parietal cortex. Brain. 2015; 138: 428–39.

6) Tanaka S, Takeda K, Otake Y, et al. Single session of transcranial direct current stimulation transiently increases knee extensor force in patients with hemiparetic stroke. Neurorehabil Neural Repair. 2011; 25: 565–9.

7) Sohn MK, Jee SJ, Kim YW. Effect of transcranial direct current stimulation on postural stability and lower extremity strength in hemiplegic stroke patients. Ann Rehabil Med. 2013 37: 759–65.

8) Fulk GD, He Y, Boyne P, Dunning K. Predicting home and community walking activity poststroke. Stroke. 2017; 48(2): 406–11.

9) Grecco LA, Duarte NA, Zanon N, et al. Effect of a single session of transcranial direct-current stimulation on balance and spatiotemporal gait variables in children with cerebral palsy: a randomized sham-controlled study. Braz J Phys Ther. 2014; 18(5): 419–27.

10) Kaski D, Dominguez RO, Allum JH, et al. Combining physical training with transcranial direct current stimulation to improve gait in Parkinson’s disease: a pilot randomized controlled study. Clin Rehabil. 2014; 28(11): 1115–24.

11) Takakusaki K. Functional neuroanatomy for posture and gait control. J Mov Disord. 2017; 10: 1–17.

12) Simonetti D, Zollo L, Milighetti S, et al. Literature review on the effects of tDCS coupled with robotic therapy in post stroke upper limb rehabilitation. Front Hum Neurosci. 2017; 23; 11: 268.

13) Làdavas E, Giulietti S, Avenanti A, et al. a-tDCS on the ipsilesional parietal cortex boosts the effects of prism adaptation treatment in neglect. Restor Neurol Neurosci. 2015; 33(5): 647–62.

14) Galletta EE, Conner P, Vogel-Eyny A, et al. Use of tDCS in aphasia rehabilitation: a systematic review of the behavioral interventions implemented with noninvasive brain stimulation for language

recovery. Am J Speech Lang Pathol. 2016; 25(4S): S854–67.

15) Geroin C, Picelli A, Munari D, et al. Combined transcranial direct current stimulation and robot-assisted gait training in patients with chronic stroke: a preliminary comparison. Clin Rehabil. 2011; 25: 537–28.

16) Takeuchi N, Izumi S. Rehabilitation with poststroke motor recovery: a review with a focus on neural plasticity. Stroke Res Treat. 2013; 1: 1–13.

17) Matsunaga K, Maruyama A, Fujiwara T, et al. Increased cortico spinal excitability after 5Hz rTMS over the human supplementary motor area. J. Physiol. 2005; 562; 295–306.

18) Kaski D, Dominguez RO, Allum JH, et al. Improving gait and balance in patients with leukoaraiosis using transcranial direct current stimulation and physical training: an exploratory study. Neurorehabil Neural Repair. 2013; 27; 864–71.

19) Kaski D, Quadir S, Patel M, et al. Enhanced locomotor adaptation aftereffect in the “broken escalator” phenomenon using anodal tDCS. J Neurophysiol. 2012; 107; 2493–2505.

20) Danzl MM, Chelette KC, Lee K, et al. Brain stimulation paired with novel locomotor training with robotic gait orthosis in chronic stroke: a feasibility study. NeuroRehabilitation. 2013; 33: 67–76.

21) Varghese JP, Merino DM, Beyer KB, McIlroy WE. Cortical control of anticipatory postural adjustments prior to stepping. Neuroscience. 2016; 313: 99–109.

22) Kirimoto H, Yoshida S, Matsumoto T, et al. The effects of cathodal transcranial direct current stimulation of the supplementary motor area on the function of anticipatory postural adjustments. Clin Neurophysiol. 2013; 124(10): 98–99.

23) Jacobs JV, Lou JS, Kraakevik JA, Horak FB. The supplementary motor area contributes to the timing of the anticipatory postural adjustment during step initiation in participants with and without Parkinson’s disease. Neuroscience. 2009; 164(2): 877–85.

24) Oyake K, Yamaguchi T, Sugasawa M, et al. Validity of gait asymmetry estimation by using an accelerometer in individuals with hemiparetic stroke. J Phys Ther Sci. 2017; 29(2): 307–11.

25) Fujimoto H, Mihara M, Hattori N, et al. Cortical changes underlying balance recovery in patients with hemiplegic stroke. Neuroimage. 2014; 15; 85: 547–54.

26) Tahtis V, Kaski D, Seemungal BM. The effect of single session bi-cephalic transcranial direct current stimulation on gait performance in sub-acute stroke: a pilot study. Restor Neurol Neurosci. 2014; 32(4): 527–32.

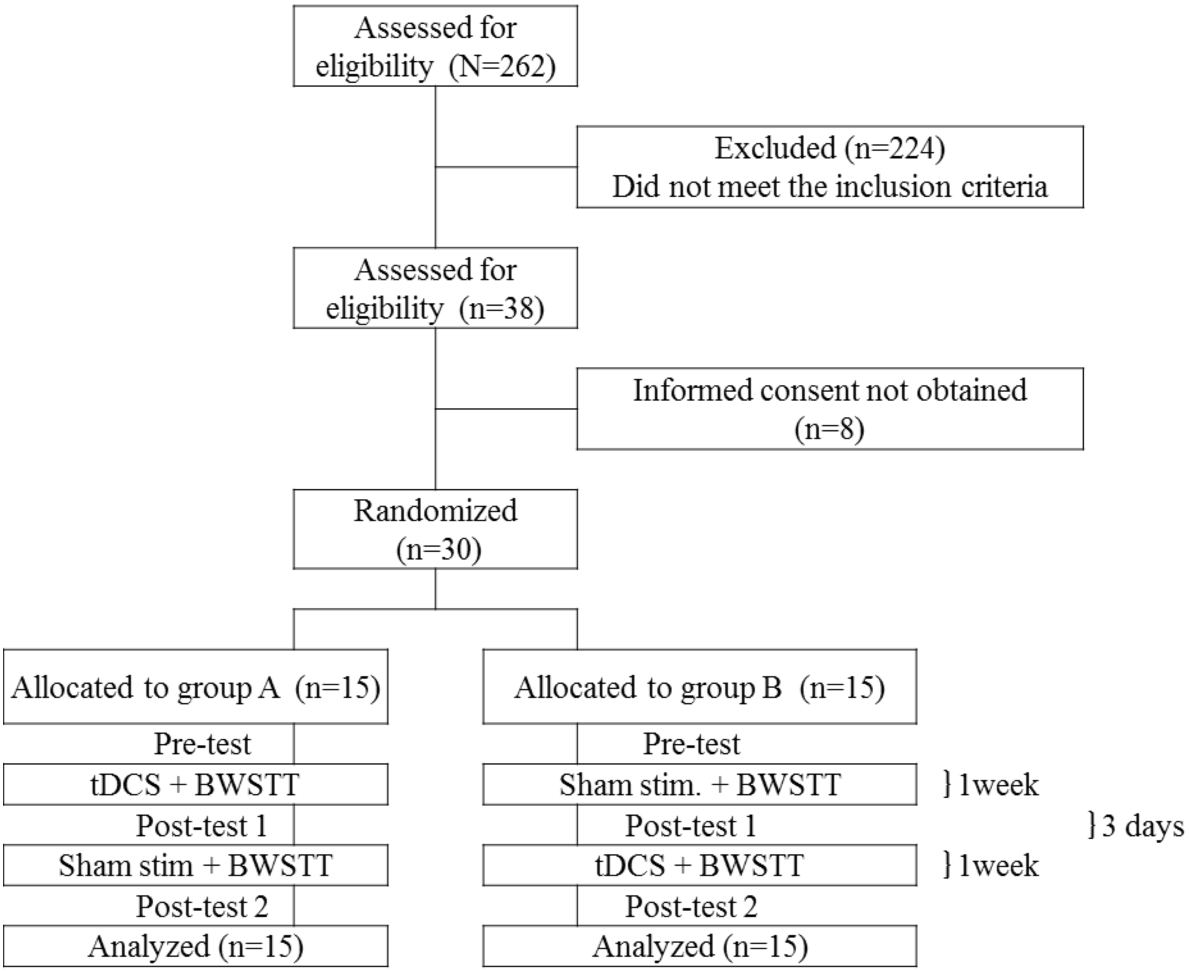
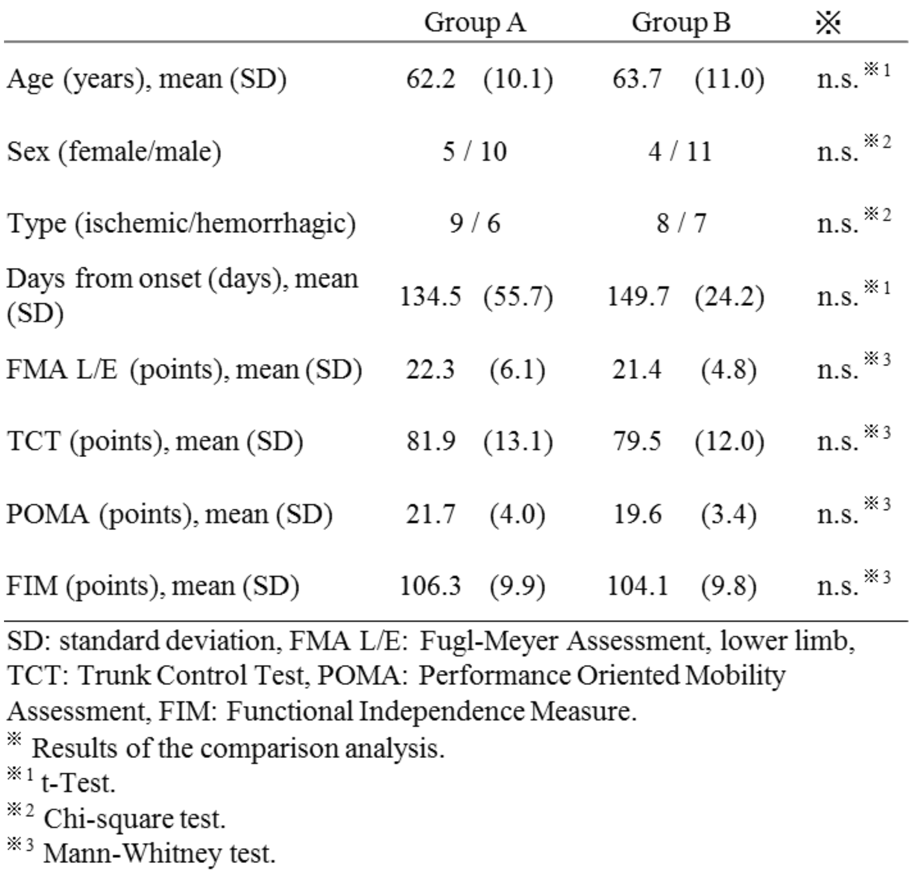


Fig. 1. Flowchart of patient participation and study.

Table 1. Participants demographic and clinical data



	Group A		Group B		※
Age (years), mean (SD)	62.2	(10.1)	63.7	(11.0)	n.s.※1
Sex (female/male)	5 / 10		4 / 11		n.s.※2
Type (ischemic/hemorrhagic)	9 / 6		8 / 7		n.s.※2
Days from onset (days), mean (SD)	134.5	(55.7)	149.7	(24.2)	n.s.※1
FMA L/E (points), mean (SD)	22.3	(6.1)	21.4	(4.8)	n.s.※3
TCT (points), mean (SD)	81.9	(13.1)	79.5	(12.0)	n.s.※3
POMA (points), mean (SD)	21.7	(4.0)	19.6	(3.4)	n.s.※3
FIM (points), mean (SD)	106.3	(9.9)	104.1	(9.8)	n.s.※3

SD: standard deviation, FMA L/E: Fugl-Meyer Assessment, lower limb, TCT: Trunk Control Test, POMA: Performance Oriented Mobility Assessment, FIM: Functional Independence Measure.

※ Results of the comparison analysis.

※1 t-Test.

※2 Chi-square test.

※3 Mann-Whitney test.

Table 2. Changes in primary and secondary outcomes

Test	Group	Pre-test mean (SD)	Post-test 1 mean (SD)	Post-test 2 mean (SD)	F value	p Value	Effect size
		＊ p<0.001					
10MWT (sec)	A	17.2 (7.5)	14.0 (5.7)	13.2 (5.5)	Main effect $F_{1.2, 34.3}=35.2$	$p<0.001$	$\eta^2=0.541$
	B	17.4 (5.7)	16.3 (5.1)	14.4 (4.0)	Interaction $F_{1.2, 34.3}=3.2$	$p=0.046$	$\eta^2=0.396$
			＊ p=0.001				
		＊ p<0.001					
TUG (sec)	A	21.6 (12.8)	17.0 (8.6)	17.0 (9.4)	Main effect $F_{1.3, 36.8}=26.1$	$p<0.001$	$\eta^2=0.557$
	B	21.5 (7.1)	20.1 (6.1)	17.9 (5.2)	Interaction $F_{1.3, 36.8}=3.9$	$p=0.026$	$\eta^2=0.100$
			＊ p<0.001				
FMA L/E (points)	A	22.3 (6.1)	22.9 (5.5)	23.1 (5.5)	Main effect $F_{1.4, 39.3}=12.8$	$p<0.001$	$\eta^2=0.313$
	B	21.4 (4.8)	21.7 (4.6)	21.9 (4.6)	Interaction $F_{1.4, 39.3}=1.4$	$p=0.262$	$\eta^2=0.046$
TCT (points)	A	81.9 (13.1)	86.1 (10.0)	87.0 (9.5)	Main effect $F_{1.2, 33.2}=12.1$	$p=0.001$	$\eta^2=0.314$
	B	81.2 (13.8)	83.7 (11.8)	86.1 (10.0)	Interaction $F_{1.2, 33.2}=1.1$	$p=0.308$	$\eta^2=0.016$
POMA (points)	A	21.7 (4.0)	22.5 (3.5)	22.9 (2.7)	Main effect $F_{2, 56}=12.8$	$p<0.001$	$\eta^2=0.301$.
	B	19.6 (3.4)	19.8 (3.3)	20.4 (2.8)	Interaction $F_{2, 56}=0.46$	$p=0.634$	$\eta^2=0.039$

SD: Standard deviation, 10MWT: 10-Meter Walk Test, TUG, Timed Up and Go Test, FMA L/E: Fugl-Meyer Assessment, lower limb, TCT: Trunk Control Test, POMA: Performance Oriented Mobility Assessment.

＊ Simple main effect analysis: Bonferroni's post hoc test, $p<0.05$.