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Clin Rehabil published online 14 March 2011
DOI: 10.1177/0269215510389497

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CLINICAL REHABILITATION

Clinical Rehabilitation
00(0) 1–12

DOI: 10.1177/0269215510389497
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Combined transcranial direct current stimulation and robot-assisted gait training in patients with chronic stroke: a preliminary comparison

Christian Geroin[1], Alessandro Picelli[1], Daniele Munari[1], Andreas Waldner[2,3], Christopher Tomelleri[2] and Nicola Smania[1,4]

Abstract

Objective: To evaluate whether robot-assisted gait training combined with transcranial direct current stimulation is more effective than robot-assisted gait training alone or conventional walking rehabilitation for improving walking ability in stroke patients.

Design: Pilot randomized clinical trial.

Setting: Rehabilitation unit of a university hospital.

Subjects: Thirty patients with chronic stroke.

Interventions: All patients received ten 50-minute treatment sessions, five days a week, for two consecutive weeks. Group 1 ($n = 10$) underwent a robot-assisted gait training combined with transcranial direct current stimulation; group 2 ($n = 10$) underwent a robot-assisted gait training combined with sham transcranial direct current stimulation; group 3 ($n = 10$) performed overground walking exercises.

Main measures: Patients were evaluated before, immediately after and two weeks post treatment. Primary outcomes: six-minute walking test, 10-m walking test.

Results: No differences were found between groups 1 and 2 for all primary outcome measures at the after treatment and follow-up evaluations. A statistically significant improvement was found after treatment in performance on the six-minute walking test and the 10-m walking test in favour of group 1 (six-minute walking test: 205.20 ± 61.16 m; 10-m walking test: 16.20 ± 7.65 s) and group 2 (six-minute walking test: 182.5 ± 69.30 m; 10-m walking test: 17.71 ± 8.20 s) compared with group 3 (six-minute walking test: 116.30 ± 75.40 m; 10-m walking test: 26.30 ± 14.10 s). All improvements were maintained at the follow-up evaluation.

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Conclusions: In the present pilot study transcranial direct current stimulation had no additional effect on robot-assisted gait training in patients with chronic stroke. Larger studies are required to confirm these preliminary findings.

Keywords
Stroke, rehabilitation, gait, brain stimulation

Received 26 July 2010; accepted 11 October 2010

Introduction

Gait impairment is a common cause of disability in patients with stroke.[1] Although it has been reported that 85% of stroke survivors recover walking function within six months after the onset, restoring the ability to walk independently with efficient velocity, endurance and gait symmetry remains one of the major goals for stroke rehabilitation during the chronic phase of illness.[2–6]

Previous studies have shown that improvement in motor performance is likely to be related to cortical reorganization occurring after stroke.[7–9] In particular, Dobkin and colleagues found that cortical motor areas encoding for distal leg movements during gait may redirect their motor commands to control more proximal segments of the lower limb after the onset, producing new patterns of muscle activity during walking.[8] Body weight-supported gait training combined with conventional rehabilitative approaches has been found to induce changes in corticomotor excitability and improve motor performance in patients with chronic stroke.[9] This is probably a consequence of a cortical reorganization, with the foot representation regaining a more usual distribution in the brain.[8]

Several neuromodulatory protocols have been proposed to induce cortical plasticity and promote motor recovery after stroke. In a recent paper, Jayaram and Stinear evaluated the effectiveness of paired associative stimulation, repetitive transcranial magnetic stimulation and transcranial direct current stimulation as potential neuromodulatory adjuvants of walking rehabilitation in patients with chronic stroke.[10] Authors reported that even if all neuromodulatory protocols increased paretic limb and decreased non-paretic limb motor excitability, no one proved to be more effective than others.[10] On the other hand, the functional implications on walking function of these results are yet to be determined.

Patients who underwent a robot-assisted walking rehabilitation programme based on the electromechanical gait trainer developed by Hesse and colleagues[11–14] have been reported to improve gait performance and maintain functional recovery at follow-up even during the chronic phase of stroke.[3,4] This is probably because robot-assisted repetition of gait-like movement allows patients to practise a complete gait cycle, achieving better symmetric and physiological walking.[4]

To the best of our knowledge, no earlier randomized controlled trial with follow-up has been carried out to evaluate the effectiveness of gait training combined with transcranial direct current stimulation during the chronic phase of stroke. Starting from our clinical experience about the usefulness of robot-assisted gait training in patients with chronic stroke for improving walking function (walking capacity and gait speed), and taking into account previous papers about the combination of robot-assisted

arm training and transcranial direct current stimulation for rehabilitation of patients with stroke,[15,16] we decided to carry out this pilot study to evaluate whether a training programme consisting of robot-assisted gait training combined with transcranial direct current stimulation could be more effective than robot-assisted gait training alone or conventional walking rehabilitation in improving walking function in patients with stroke during the chronic phase of illness.

Methods

This pilot randomized clinical trial was performed in the Neurological Rehabilitation Unit of the Azienda Ospedaliera-Universitaria Integrata of Verona, Italy. Inclusion criteria were: at least 12 months from their first unilateral ischemic stroke; age <75 years; European Stroke Scale[17] score ≥75 and ≤85; Mini Mental State Examination[18] score ≥24; ability to maintain standing position without aids for at least 5 minutes; ability to walk independently for at least 15 m with the use of walking aids (cane and orthoses). Exclusion criteria were: preceding epileptics fits; an electroencephalography suspect of elevated cortical excitability; metallic implants within the brain and previous brain surgery; medications altering cortical excitability (such as antiepileptics, neuroleptics, benzodiazepines or antidepressant) or with a presumed effect on brain plasticity (such as dopamine, fluoxetin or D-amphetamine); posterior circulation stroke; deficits of somatic sensation involving the paretic lower limb; presence of vestibular disorders or paroxysmal vertigo; presence of severe cognitive or communicative disorders; presence of other neurological or orthopaedic conditions involving the lower limbs; presence of cardiovascular comorbidity; performance of any type of rehabilitation treatment in the three months before the start of the study.

The protocol was carried out according to the Declaration of Helsinki and was approved by the Ethics Committee of the Department of Neurological, Neuropsychological, Morphological and Movement Sciences of Verona University.

All participants were outpatients and gave their informed consent for participation in the study. After baseline evaluation, patients were allocated to one of three treatment groups according to a simple software-generated randomization scheme.[19]

Each patient underwent a training programme consisting of ten 50-minute sessions (including 20 minutes of walking training and 30 minutes of lower limbs muscle strengthening and joint mobilization exercises), five days a week (from Monday to Friday) for two consecutive weeks.

Patients allocated to group 1 performed robot-assisted gait training combined with transcranial direct current stimulation. Transcranial direct current stimulation was applied via saline-soaked surface sponge electrodes (35 cm^2) connected to a constant current stimulator (Phyaction 787, Uniphy, The Netherlands). The anodal electrode was placed over the presumed leg area of the lesioned hemisphere, while the cathode was placed above the contralateral orbit of the eye (ipsilaterally to the impaired lower limb).[10,15] The stimulation intensity was set at 1.5 mA and was applied simultaneously to the robot-assisted gait training during the first 7 minutes of training.[15] After this period the stimulator was switched off, while electrodes remained in place until robot-assisted gait training ended.

The robot-assisted gait training was performed by means of the electromechanical Gait Trainer GT1 (Reha-Stim, Berlin, Germany).[3,4,14,20,21] During the robot-assisted gait training patients were supported with a harness and their feet were placed on motor-driven footplates. According to the Hesse methodology, patients received a maximum of 30% body weight relief within the first training sessions.[3,22] During the training programme, body weight support was progressively decreased. The speed was selected from 1.4 to 1.8 km/h according to the patient's

skills, while the step length was defined according to each patient's physical characteristics.

Patients allocated to group 2 performed robot-assisted gait training combined with sham transcranial direct current stimulation. During the first 7 minutes of the robot-assisted gait training, patients received sham transcranial direct current stimulation (electrodes were applied as in group 1 but the current stimulator was switched off).

Patients allocated to group 3 performed over-ground walking exercises according to the Bobath approach.[23,24]

Patients were evaluated before treatment (T_0), immediately after treatment (T_1) (primary endpoint), and two weeks after the end of treatment (T_2). All patients were evaluated by the same examiner (an experienced internal co-worker) who was not aware of the treatment received by the patients.

Primary outcome measures were the six-minute walking test[25,26] and the 10-m walking test.[27] The six-minute walking test was selected as a measure of walking capacity.[25,26] This is a validated tool evaluating some important requirements of ambulation such as submaximal endurance and dynamic balance.[26] Subjects were required to walk at their maximum speed for 6 minutes and the score was the distance covered.[25,26] They were allowed to use walking aids (cane and orthoses). Gait speed was assessed using the 10-m walking test.[27] This is a validated test requiring patients to walk on a flat hard floor at their most comfortable pace for 10 m. They were allowed to use walking aids (cane and orthoses). Scoring was walking speed.

We considered the following measures and tests as secondary outcomes.

The GAITRite system (Gold version 3.2b; CIR Systems Inc, Havertown, PA, USA) was used to evaluate spatiotemporal gait parameters.[28] To avoid the effects of acceleration and deceleration, patients were asked to ambulate along the 7.66 m GAITRite electronic walkway at their fastest speed on a 12 m course. Patients were allowed to use orthoses but not other walking aids such as a cane. Three trials of this task were conducted, with the mean of these trials calculated. Cadence, temporal symmetry ratio (ratio between paretic swing time/paretic stance time and non-paretic swing time/non-paretic stance time)[29] and ratio between single and double support duration were evaluated.

The Functional Ambulation Categories[30] were used to classify patients' locomotion ability. Score ranged from 0 (patient cannot walk or needs help from two or more persons) to 5 (patient can walk independently anywhere).

The Rivermead Mobility Index[31] was used to evaluate patients' ability to move their bodies. Scores ranged from 0 to 15 (higher scores corresponding to better performances).

The Motricity Index leg subscore[32] was used to assess the paretic limb strength in patients with stroke. The leg subtest score ranges from 1 (total paralysis) to 100 (normal strength).

The Modified Ashworth Scale[33] was used to test the muscle tone at hip adductors, quadriceps femoris and ankle plantiflexors. The Modified Ashworth Scale is a validated scale grading the resistance of a relaxed limb to rapid passive stretch in six stages (range 0–5; 0: no increase in muscle tone; 5: joint is rigid in flexion or extension).

The Kruskal–Wallis test was used to test the homogeneity between the groups before the study. The Friedman test was used to analyse changes in performance in the different evaluation sessions within each patient group. The Wilcoxon signed ranks test on the pre-/post-treatment scores and on the pre-treatment/follow-up scores for the different outcome measures were carried out in each group of patients. The Mann–Whitney *U*-test was used to compare the effect of treatment in the three patient groups. For this purpose, we computed the differences between post- and pre-treatment performance and between

follow-up and pre-treatment performance for all outcome measures. The alpha level for significance was set at $P < 0.05$. The Bonferroni correction[34] was used in multiple comparisons ($P < 0.025$). Statistical analysis was carried out using the SPSS for Windows statistical package, version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Thirty subjects (23 males and 7 females; mean age: 62.7 years; SD: 6.4 years) presenting with hemiparesis as a result of chronic stroke (mean time from onset: 26.4 months; SD: 5.5 months) were recruited from among 93 outpatients, consecutively admitted to our neurological rehabilitation unit during the period from November 2008 to November 2009. Ten patients were allocated to each group. No drop-out was observed and no adverse events occurred during the trial in any of the groups. The flow diagram of the study is reported in Figure 1.

Multiple independent-sample Kruskal–Wallis tests showed that age, education, length of illness, neurological severity and primary outcome measures were not statistically different between the three groups at T_0 evaluation. Patients' demographic and clinical characteristics are detailed in Table 1.

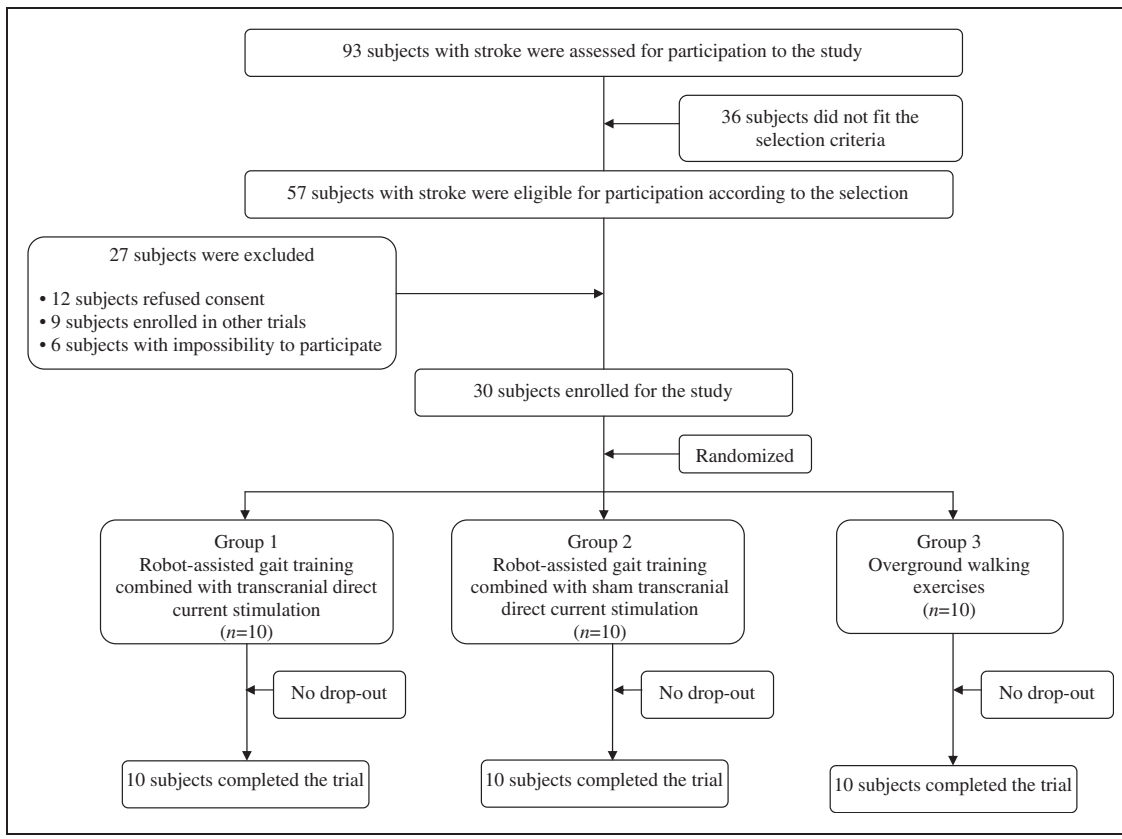

Figure 1. Flow diagram of the study.

Primary outcomes

As reported in Table 2, between-groups comparisons showed that patients in groups 1 and 2 performed significantly better than those in group 3, in all primary outcome measures at both the post-treatment and follow-up evaluations. No significant differences were found between groups 1 and 2, in all primary outcome measures at both T_1 and T_2 evaluations.

In group 1, overall significant improvements in performance in the different evaluation sessions were found in regards to all primary outcome measures (six-minute walking test:

Table 1. Demographic and clinical features of patients

Parameter	Group 1 ($n = 10$)	Group 2 ($n = 10$)	Group 3 ($n = 10$)
Age (years)			
Mean (SD)	63.6 (6.7)	63.3 (6.4)	61.1 (6.3)
Range	52–73	53–72	51–71
Sex (male/female)	8/2	6/4	9/1
Education (years)			
Mean (SD)	8.42 (3.69)	8.03 (3.48)	7.98 (3.55)
Range	3–15	3–16	2–18
Neurological severity (ESS score)			
Mean (SD)	79.6 (4.1)	79.6 (2.7)	80.6 (3.2)
Range	75–85	76–85	76–82
Disease duration (months)			
Mean (SD)	25.7 (6.0)	26.7 (5.1)	26.9 (5.8)
Range	16–34	19–33	14–34
Lesion localization (cortical/subcortical/mixed)	4/3/3	5/2/3	3/4/3

SD, standard deviation; *n*, number of patients; ESS, European Stroke Scale.

Table 2. Comparison of treatment effects between groups in primary outcome measures

		Between groups comparison (Mann–Whitney *U*-test)	
Primary outcome measures	Group comparison	After–before difference *P*-value (*Z*)	Two weeks follow-up–before difference *P*-value (*Z*)
Six-minute walking test (m)	Group 1–2	0.140 (−1.475)	0.059 (−1.891)
	Group 1–3	<0.001 (−3.798)*	<0.001 (−3.797)*
	Group 2–3	<0.001 (−3.797)*	<0.001 (−3.797)*
10-m walking test (s)	Group 1–2	0.324 (−0.985)	0.121 (−1.551)
	Group 1–3	0.001 (−3.415)*	0.001 (−3.195)*
	Group 2–3	0.002 (−3.110)*	0.009 (−2.621)*

*Significant comparison ($P < 0.05$).

$X = 20.000$, $P < 0.001$; 10-m walking test: $X = 18.667$, $P < 0.001$). As reported in Table 3, within-group comparisons showed that improvements in performance were significant at both the post-treatment and follow-up evaluations. In group 2, overall significant improvements in performance in the different evaluation sessions were found in regards to all primary outcome measures (six-minute walking test: $X = 19.538$, $P < 0.001$; 10-m walking test: $X = 12.182$, $P = 0.002$). As reported in Table 3, within-group comparisons showed that improvements in performance were significant at both the post-treatment and follow-up evaluations. In group 3 no significant changes in performance in the different evaluation sessions were found in regards to all primary outcome measures. Row data (means and standard deviations) of patients' performance at before, after and follow-up evaluations are reported in Table 3.

Secondary outcomes

No significant differences were found between group 1 and 2, in all secondary outcome measures at both T_1 and T_2 evaluations. Between-groups comparison showed that patients in groups 1 and 2 performed significantly better than those in group 3 in all spatiotemporal gait parameters at both the post-treatment (groups 1–3 comparison: cadence: $P = 0.001$, temporal symmetry ratio: $P = 0.021$, ratio between single and double support duration: $P = 0.002$; groups 2–3 comparison: cadence: $P < 0.001$, temporal symmetry ratio: $P = 0.003$, ratio between single and double support duration: $P = 0.001$) and follow-up (groups 1–3 comparison: cadence: $P = 0.001$, temporal symmetry ratio: $P = 0.001$, ratio between single and double support duration: $P = 0.001$; groups 2–3 comparison: cadence: $P < 0.001$, temporal symmetry ratio: $P = 0.001$, ratio between single and double support duration: $P = 0.021$) evaluations. Moreover patients in groups 1 and 2 performed significantly better than those in group 3 in the Functional Ambulation Categories, Rivermead Mobility

Table 3. Comparison of treatment effects within group in primary outcome measures

Primary outcome measures	Group	Before Mean (SD)	After Mean (SD)	Two weeks follow-up Mean (SD)	Within-group comparison (Wilcoxon signed ranks test)		95% Confidence interval	
					After–before *P*-value (*Z*)	Two weeks follow-up–before *P*-value (*Z*)	After–before Mean (LB; UB)	Two weeks follow-up–before Mean (LB; UB)
Six-minute walking test (m)	Group 1	162.90 (52.09)	205.20 (61.16)	214.90 (59.76)	0.005 (−2.805)*	0.005 (−2.803)*	−42.30 (−56.80; −27.79)	−52.00 (−66.84; −37.15)
	Group 2	156.10 (62.90)	182.5 (69.30)	189.60 (71.30)	0.005 (−2.803)*	0.005 (−2.803)*	−24.40 (−37.48; −15.31)	−33.50 (−45.37; −21.62)
	Group 3	116.80 (75.20)	116.30 (75.40)	116.70 (76.50)	0.339 (−0.957)	0.833 (−0.211)	−0.50 (−0.63; 1.63)	0.10 (−2.17; 2.37)
10-m walking test (s)	Group 1	18.24 (8.24)	16.20 (7.65)	15.82 (7.57)	0.005 (−2.803)*	0.005 (−2.807)*	2.04 (1.32; 2.75)	2.42 (1.59; 3.24)
	Group 2	19.20 (8.70)	17.71 (8.20)	17.65 (8.20)	0.007 (−2.705)*	0.007 (−2.701)*	1.49 (0.91; 2.07)	1.54 (0.95; 2.14)
	Group 3	26.32 (14.70)	26.30 (14.10)	26.59 (15.60)	0.766 (−0.298)	0.330 (−0.975)	0.20 (−0.55; 0.59)	−0.27 (−1.23; −0.69)

SD, standard deviation; LB, lower bound; UB, upper bound.
*Significant comparison ($P < 0.05$).

Index and Motricity Index leg subscore at both the post-treatment (groups 1–3 comparison: Functional Ambulation Categories: $P < 0.001$, Rivermead Mobility Index: $P < 0.001$, Motricity Index leg subscore: $P < 0.001$; groups 2–3 comparison: Functional Ambulation Categories: $P < 0.001$, Rivermead Mobility Index: $P < 0.001$, Motricity Index leg subscore: $P < 0.001$) and follow-up (groups 1–3 comparison: Functional Ambulation Categories: $P < 0.001$, Rivermead Mobility Index: $P < 0.001$, Motricity Index leg subscore: $P < 0.001$; groups 2–3 comparison: Functional Ambulation Categories: $P < 0.001$, Rivermead Mobility Index: $P < 0.001$, Motricity Index leg subscore: $P < 0.001$) evaluations.

As reported in Table 4, within-group comparisons showed that improvements in performance were significant in groups 1 and 2 for all spatio-temporal gait parameters, Functional Ambulation Categories, Rivermead Mobility Index and Motricity Index leg subscore at both the post-treatment and follow-up evaluations. In group 3, within-group comparisons showed that improvements in performance were significant only for the ratio between single and double support duration and Motricity Index leg subscore at both the post-treatment and follow-up evaluations (Table 4).

Discussion

With regard to the main aim of the study, our results showed that anodal transcranial direct current stimulation has no additional effect on

Table 4. Comparisons of treatment effects within group in secondary outcome measures

		Within-group comparisons (Wilcoxon signed ranks test)	
Secondary outcome measures	Group	After–before difference (SD)	Follow-up–before difference (SD)
Cadence (cycles/min)	Group 1	9.78 (6.82)*	12.31 (7.04)*
	Group 2	9.33 (12.62)*	12.73 (13.08)*
	Group 3	(−) 3.2 (8.77)	(−) 3.11 (9.69)
Temporal symmetry ratio	Group 1	(−) 0.27 (0.06)*	(−) 0.30 (0.06)*
	Group 2	(−) 0.35 (0.09)*	(−) 0.40 (0.09)*
	Group 3	(−) 0.03 (0.11)	0.07 (0.12)
Single-double support duration ratio (m/s)	Group 1	0.50 (0.13)*	0.47 (0.13)*
	Group 2	0.68 (0.20)*	0.55 (0.19)*
	Group 3	0.20 (0.05)*	0.10 (0.03)*
Functional Ambulation Categories (0–5)	Group 1	1.00 (0.21)*	1.00 (0.21)*
	Group 2	1.20 (0.20)*	1.20 (0.20)*
	Group 3	0.00 (0.13)	0.00 (0.13)
Rivermead Mobility Index (0–15)	Group 1	4.80 (0.58)*	4.80 (0.68)*
	Group 2	3.90 (0.77)*	4.40 (0,73)*
	Group 3	0.40 (0.56)	0.40 (0.56)
Motricity Index leg subscore (0–100)	Group 1	27.00 (2.36)*	28.2 (2,37)*
	Group 2	27.00 (2.18)*	31.80 (0.79)*
	Group 3	8.50 (1.83)*	8.50 (1.83)*

SD, standard deviation.
*Significant comparison ($P < 0.05$).

robot-assisted gait training in patients with chronic stroke.

Balanced transcallosal inhibition sustains symmetrical corticomotor excitability in healthy subjects.[35] After stroke the contralesional hemisphere has been reported to become hyperexcitable, increasing the transcallosal inhibition of the lesioned hemisphere and suppressing recovery of the ipsilesional motor cortex.[36,37] Transcranial direct current stimulation has been found to modulate (inhibiting or facilitating) cortical excitability in order to induce plastic changes within the network of sensorimotor areas of the cortex and, at the same time, improve dexterity of the affected hand in patients with stroke.[38] In particular, two pilot studies investigated the effectiveness of anodal transcranial direct current stimulation combined with robot-assisted arm training in patients with stroke, reporting encouraging results about the usefulness of this approach to promote robotic practice-dependent plasticity and motor functional improvements.[15,16] With regard to the lower limb, anodal transcranial direct current stimulation proved to be effective in increasing the excitability of the leg corticospinal tract and decreasing contralesional motor cortex excitability as a result of an increased transcallosal inhibition from the ipsilesional to the contralesional hemisphere.[10,39] However, the functional implications of restoring the symmetry of between-hemisphere lower limb excitability are still the object of debate.[10,40] To the best of our knowledge, this is the first study that has evaluated the application of anodal transcranial direct current stimulation as a method to enhance the effect of robot-assisted gait training in patients with chronic stroke; unfortunately, our results do not support the effectiveness of this innovative approach.

One possible explanation could be found in the different types of neuronal control of the upper and lower limb. Indeed, the regulation of walking requires a close coordination of muscle activation between the two legs that it is thought to be mainly determined at spinal level according to the 'half centre' model.[41] In this model, the basic locomotor rhythm and alternating activity in lower limbs flexors and extensors needed for locomotion is considered to be produced by the activity of central pattern generators (CPG) with the mutual inhibition of flexor and extensor half centres.[41–43] Moreover, a task-dependent neuronal coupling has been observed between lower and upper limbs which sustains the interlimb coordination during locomotor activities through propriospinal neuronal circuits.[41] By contrast, during skilled hand movements, the propriospinal system has been suggested to be functionally suppressed by stronger direct cortico-motoneuronal connections to upper limb muscles, which would determine the degree of manual dexterity.[41]

With regard to cortical influences in human gait, patients with chronic stroke were seen to have a practice-induced representational plasticity (characterized, for example, by the foot representation regaining a more usual distribution) associated with gains in speed, capacity, motor control and kinematics for walking during gait rehabilitation.[8] Moreover, considering that during the execution of voluntary tasks, which require conscious control of muscle activation, M1 motoneurons appear to equally control the segmental spinal motor pools of the flexors and extensors, in literature it has been suggested that activation of M1 is coupled to the timing of spinal locomotor activity in a task-dependent way.[8,44]

On the basis of all these physiological considerations, we argue that the lack of additional effects of transcranial direct current stimulation on robot-assisted gait training seen in our patients could be mainly ascribed to the peculiar neural organization of locomotion, consisting of both cortical (M1) and spinal (CPG) neural control. In particular, the repetitive robot-assisted walking activity could be responsible for a likely prevalence of sensory proprioceptive feedback on supraspinal inputs, leading to a greater activation of lower neural control of locomotion and more symmetrical hemispheric stimulation, with a relatively inefficacy of transcranial direct current stimulation as conversely

further demonstrated in rehabilitation of the upper limb (which have a more direct and unilateral cortico-motoneuronal representation).[41] Furthermore, walking automatisms, which are mainly determined at a spinal level (CPG), could not be greater functionally influenced by cortical activation due to anodal transcranial direct current stimulation.

Another possible explanation of the results may be found in the transcranial direct current stimulation methods. Indeed, considering the close proximity of the two lower limb motor cortices either side of the central fissure, it is reasonable that cortical currents were induced in both brain hemispheres, extending facilitatory modulation even to the contralesional side.[40] Another methodological consideration could involve the stimulation intensity. Given that robot-assisted gait training leads to a more symmetrical activation of the motor cortex than conventional treatment, it is reasonable that more intensive transcranial stimulation currents would be needed to produce additional effects on locomotion rehabilitation. Finally, the possibility of inaccuracy in anode placement (partially bridging the central fissure) must be considered.

Restoration of walking ability is a major goal in the rehabilitation of patients with stroke, even during the chronic phase of illness.[4] With regard to walking performance, the results showed that motor abilities and gait characteristics improved after treatment and maintained the discharge level at two-week follow-up in both robot-assisted gait training groups rather than conventional walking rehabilitation group. Consistent with previous findings, patients with chronic stroke showed improvement in walking ability and functional independence after an intensive robot-assisted gait training programme based on the electromechanical gait trainer with body-weight support.[3,4,45] Residual descending motor pathways have been proposed to play a role in improving gait in patients with chronic stroke who undergo robot-assisted walking rehabilitation.[45] Moreover, repetitive robot-assisted training of locomotion induces changes in corticomotor excitability and leads to potential brain reorganization in patients with chronic stroke.[9] Previous studies suggest that bilateral ambulation training is the key element in stimulating the activation of brain hemispheres in order to improve activity and functional ability of the paretic lower limb.[3,9]

As to the clinical significance of the effects of robot-assisted gait training, it is important to note that improvements in walking capacity and gait speed are relevant from a functional point of view. In fact, recovery of walking capacity is closely related to functional capacity and quality of life in patients with stroke,[46] while improvements of gait speed are related to a more physiological walking with less variability of spatiotemporal parameters.[45]

Another interesting aspect of this pilot study regards the placebo effect of sham transcranial direct current stimulation. Considering that patients who performed robot-assisted gait training also underwent transcranial direct current stimulation (genuine or sham) it is plausible that placebo effect could have played a role in our findings. Unfortunately, we did not perform any neurophysiological evaluation, such as motor-evoked potential recording, that could provide a measure of corticomotor excitability and information about the placebo effect of the sham stimulation. Future research should combine clinical and neurophysiological outcome measures in order to obtain a further validation of findings.

This is a pilot study with several limitations and it should be emphasized that the strength of our conclusions is limited. First, the sample size was small. The population size may have hindered evaluation of the effects of transcranial direct current stimulation combined with robot-assisted gait training. In order to further validate our findings, randomized controlled trials involving a larger subject population are needed. Taking into account a previous study about robot-assisted gait training in stroke patients,[3] we estimate that 54 subjects would provide 90% power to detect a significant difference between groups in the six-minute walking

test. Second, the number of transcranial direct current stimulation parameters examined was limited. Our protocol was made of 7-minutes, 1.5 mA transcranial direct current stimulation sessions. Future studies should evaluate the effectiveness of longer and more intensive sessions, using smaller electrodes aimed at increasing transcranial direct current stimulation spatial resolution. Third, there was a lack of comparison with other transcranial stimulation modalities (such as paired associative stimulation and repetitive transcranial magnetic stimulation) and rehabilitation approaches other than the Bobath one.

Clinical messages

- Anodal transcranial direct current stimulation seems to have no additional effect on robot-assisted gait training in patients with chronic stroke.
- Robot-assisted gait training confirms to be more effective than conventional training in enhancing walking ability in patients with chronic stroke.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare that they have no conflict of interest related to the publication of this manuscript.

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