FES-induced Cycling Improves Locomotion in Post-Acute Ischemic Stroke Patients: a Randomized Controlled Trial

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Abstract

A recent double-blind randomized controlled trial strongly supported the hypothesis that FES- cycling training applied in the post-acute phase after stroke could play a crucial role in promoting motor recovery. This study presents a subgroup analysis on 20 ischemic stroke patients, mainly focusing on the benefits achieved in cycling performance and walking speed. The treatment consisted of 20 sessions lasting 25 minutes each. Participants were randomized into two groups performing FES- cycling or placebo FES-cycling training. Patients were evaluated before training, after training, and at 3- to 5-month follow-up visits through a voluntary pedaling test and a 50-meter walking test. No significant differences were found between groups at baseline. Repeated-measures ANOVA revealed a significant increase in gait speed after training and at follow-up assessments for FES-treated patients. A main effect favoring FES group was demonstrated by repeated-measures ANCOVA in terms of gait speed, unbalance in mechanical work between paretic and nonparetic quadriceps during cycling, and correlation between the torque profile of the paretic leg and the mean profile of a group of healthy volunteers performing the same pedaling test. The study showed that FES-cycling training is particularly effective in improving cycling and walking ability on post-acute ischemic stroke patients.

Keywords*: FES cycling, neurorehabilitation, motor relearning, locomotion, stroke, randomized controlled trial.*

Introduction

Restoration of walking is considered the main goal of post-stroke lower limb rehabilitation. Since the 1990s, Functional Electrical Stimulation (FES) has been increasingly used in post-stroke gait rehabilitation, given some evidence of its effectiveness in improving motor and walking ability [1]. A safe and economic alternative to FES-induced gait training is the employment of FES synchronized to the cycling movement, which entails a coordinated activation of the lower limb muscles, approximating the cyclic movements of locomotion. The feasibility of FES-induced cycling training on post-acute [2, 3] and chronic [4] stroke patients has been recently shown. These studies suggest that FES-cycling is effective in improving muscle strength [2], cycling smoothness [3], and peak pedaling power [4]. Within this framework, a fundamental open question is whether FES-mediated training on a cycle-ergometer translates to improvements in overground locomotion. Because of the similarities between cycling and walking and the afferent-efferent stimulation provided by FES, it might be hypothesized that FES-induced cycling applied in the post-acute phase could play a crucial role in promoting motor recovery and improving locomotion. This hypothesis has been recently verified by a double-blind randomized controlled [5], whose results strongly supported that a 4-week treatment of FES-induced cycling improves motor recovery and walking ability in post-acute hemiparetic patients.

The present study investigated further the results of that work [5], analyzing the subgroup of ischemic stroke patients, being ischemic stroke the main cause of hemiparesis.

Methods

Participants and design

Twenty patients, diagnosed with a first time ischemic stroke less than 6 months before study onset, were recruited for the study. Additional inclusion criteria were: sufficient cognition to perform active standard rehabilitation, able to sit up to 30 minutes, joint mobility ranges that would not preclude pedaling, and low spasticity in the lower limb muscles (Modified Ashworth Score<2). Exclusion criteria were: cardiac pacemakers, allergy to electrodes, and an inability to tolerate stimulation. All patients received an information sheet and gave their written informed consent. The research protocol was approved by the medical ethics committee of the Valduce Hospital. Normality ranges for the outcome measures related to the pedaling test were computed on a group of 6 healthy volunteers (age 29.0 ± 6.5 years, weight 61.5 ± 13.6 kg and height 171.3 ± 11.0 cm).

A double-blind randomized clinical trial was conducted. Patients were randomly allocated into 2 groups receiving cycling training synchronized to FES (FES group), or passive cycling training with FES placebo (placebo group). Both patients and assessors were unaware of group assignment. Subjects were tested before and after training and in follow-up visits, which took place from 3 to 5 months after the end of the treatment.

Intervention and outcome measures

All participants were trained 5 times a week, receiving a total of 20 sessions lasting 25 minutes each. During training, patients were asked not to pedal voluntarily. In addition to the assigned group treatment, each subject performed their own standard rehabilitation program, which consisted of 3 hours a day of physical therapy.

Primary outcome measure consisted of gait speed, computed by timing a walk of 50 meters. Subjects were asked to walk at a self-selected speed, using walking aids if necessary. Gait speed was regarded as zero if the test was not completed. Furthermore, a voluntary pedaling test was performed. A motorized cycle-ergometer customized with resistance strain gauges on the crank arms was used to measure the torque generated by each leg during pedaling. Each trial consisted of 1 minute of passive cycling, followed by 2 minutes of voluntary pedaling. The crank angle and the torque signals were acquired at a frequency of 200 Hz. The active torque profiles during voluntary pedaling were estimated by subtracting the passive torques from the measured total torques. The contribution of the quadriceps and hamstrings were separated by means of a kinematics analysis carried out on the group of healthy volunteers. The work computed as the integral of the active torque during knee extension (144°-320° for the right leg, being 0° the angle corresponding to the maximum flexion of the left hip) was related to the quadriceps contribution. Analogously, the work computed during knee flexion (320°-144° for the right leg) corresponded to the hamstring contribution. The outcome measures were: the work produced by the paretic quadriceps (W_{QUAD}) and hamstrings (W_{HAM}), the unbalance in the work between paretic and non paretic quadriceps (U_{QUAD}) and hamstrings (U_{HAM}), and the correlation between the torque profile of the paretic leg and the mean profile obtained by healthy subjects, computed as zero lag of the normalized covariance function. Please consider that the unbalance ranged from 0% (identical works) to 100% (paretic work ≤0).

Statistical Analysis

A t-test was used to compare the two groups in terms of age, time since stroke, and gait speed at baseline. The effect of time was assessed by using repeated-measures analysis of variance (ANOVA) and the effect of group by using repeated-measures analysis of covariance (ANCOVA) with baseline as covariate ($P<0.05$). If the ANCOVA test revealed a significant effect based on pooled scores (post-training and follow-up), post-hoc analysis using ANCOVA dealing separately with post-training and follow-up scores was performed.

Results

Table 1 outlines participants' details at baseline: there were no significant differences between groups in terms of demographics variables and gait speed at baseline; participants allocated to the FES group showed a better score in terms of gait speed, although no significant difference was found.

Table 1 Participants' details at baseline

	Placebo *n=8*	**FES** *n=10*	**P**
age, years *	57(11)	61 (10)	0.42 ‡
time since stroke, days *	48 (31)	38 (31)	0.52 ‡
gender (M/F)	5/3	7/3	
hemiparesis side (right/left)	4/4	5/5	
50-meter walking test (able/not able)	2/6	3/7	
Gait speed (m/s) *	0.05 (0.09)	0.17 (0.30)	0.28 ‡

* Mean (standard deviation, SD) ‡ t-test for independent samples

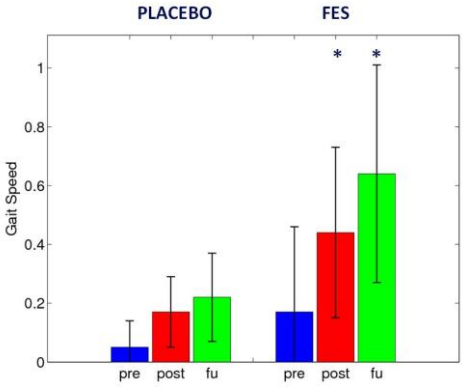

Fig. 1: Gait speed results. * indicates difference from baseline to post-training and baseline to follow-up.

Repeated-measures ANOVA ($P<0.05$) revealed significant increases in gait speed after training and at follow-up for FES-treated patients, while no differences were found for the placebo group. The ANCOVA based on pooled scores showed a significant difference between group in favor of FES-treated patients ($P=0.02$) and the post-hoc analysis revealed that the difference between

groups was statistically significant only at follow-up (P=0.02).

Table 2 reports the results of the pedaling test. It can be noticed that all scores obtained by patients were considerably different from the ones computed on healthy subjects. No significant difference was found between pre- and post-training scores for both groups. However, a main effect favoring FES group was showed by ANCOVA in terms of W_{QUAD}, U_{QUAD} and correlation of torque profiles.

Table 2 Comparison of Pre-, Post-training and Follow-up Pedaling Assessment tests

	Group	Baseline*	Post-training*	Follow-up*	P † (pre vs post)	P † (pre vs fu)	P † (post vs fu)	P ‡	P § (post)	P § (fu)
	Placebo	87 (30)	91 (14)	87 (14)	0.99	1.00	0.99			
U_{QUAD} (%)	FES	62 (31)	52 (39)	44 (33)	0.64	0.07	0.79	*0.02*	0.06	*<0.01*
	Healthy	2 (2)								
	Placebo	86 (15)	86 (14)	86 (10)	1.00	1.00	1.00			
U_{HAM} (%)	FES	85 (24)	68 (35)	69 (35)	0.34	0.30	1.00	0.13		
	Healthy	6 (4)								
	Placebo	1.1 (4.6)	0.6 (1.4)	0.3 (2.9)	0.99	0.99	0.99			
W_{QUAD} (Nm)	FES	6.3 (7.7)	10.8 (10.6)	12.1 (10.1)	0.37	0.13	0.99	*0.04*	0.08	*0.03*
	Healthy	21.1 (3.6)								
	Placebo	0.9 (1.1)	0.9 (0.7)	1.2 (1.4)	1.00	0.99	0.99			
W_{HAM} (Nm)	FES	0.8 (1.9)	3.2 (4.6)	3.0 (3.8)	0.23	0.33	0.99	0.17		
	Healthy	14.7 (3.5)								
	Placebo	-0.13 (0.42)	-0.19 (0.46)	-0.19 (0.37)	0.99	0.99	1.00			
Correlation	FES	-0.01 (0.46)	0.42 (0.54)	0.48 (0.39)	0.11	*0.05*	0.99	*0.01*	*0.02*	*<0.01*
	Healthy	0.79 (0.21)								

* Mean (SD) † Repeated-measures ANOVA ‡ Repeated-measures ANCOVA with baseline as covariate (pooled-score) § ANCOVA with baseline as covariate (post-training or follow-up)

Discussion

Comparing the results obtained on the whole population of patients included in [5] to the results on the subgroup of ischemic stroke patients here presented, it seems that FES-cycling training is even further effective on this category of patients. Indeed, a significant difference was found between groups in favor of FES-treated patients, although this difference was more evident at follow-up. Furthermore, the analysis of the pedaling test permitted to investigate the mechanisms that contributed to such an improvement of walking ability: the increase of the work produced by the paretic quadriceps and the improvement in terms of U_{QUAD} suggested a strengthen of the paretic leg which probably made the patients walk faster. Finally, the treatment had no effect on the recovery of hamstring, which remains an unsolved aspect of the post-stroke lower limb rehabilitation.

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