10th Annual Conference of the International FES Society
July 2005 – Montreal, Canada

Increased cortical excitability following one session of FET

Barsi G, Popovic DB, Sinkjær T, Grey MJ

Center for Sensory-Motor Interaction, Department of Health Science and Technology, Aalborg University

mg@smi.auc.dk

Abstract

The purpose of this study was to investigate if FET produces a greater increase in cortical excitability than either electrical stimulation (ES) or voluntary (VOL) training alone in able-bodied volunteers. Cortical excitability was assessed with transcranial magnetic stimulation (TMS) by constructing a stimulus-response input-output curve with motor evoked responses of the finger flexor muscles. A 20-minute FET session produced an 83% increase in the maximum height of the input-output curve, whereas ES and VOL produced no increase in cortical excitability. These results suggest that the combination of ES and voluntary exercise might lead to better recovery than either ES or voluntary exercise alone. Furthermore, FET might enhance motor recovery following stroke by increasing cortical excitability, thus promoting cortical plasticity.

1. INTRODUCTION

The observation of carry-over effects with Functional Electrical Stimulation has led to the development of electrical stimulation (ES) as a therapeutic intervention for the treatment of stroke [1;2]. One treatment, Functional Electrical Therapy (FET) combines intensive voluntary exercise with patterned ES of specific muscle groups to mimic the normal activation of able-bodied humans [1-3].

Results from recent clinical studies have shown promise for the use of FET in the acute phase stroke rehabilitation of upper-limb motor function [1,3]. However, the physiological mechanisms that promote this recovery remain unknown. Both aspects of FET, motor training and ES, have independently been shown to produce cortical reorganisation [e.g. 4;5]. The combination of ES and voluntary motor training (VOL) also produces changes in cortical excitability in the tibialis anterior [6-8]. This suggests that one of the primary benefits of FET might be that it promotes functional motor recovery by strengthening corticospinal circuitry.

The apparent carry-over effects of FES suggest that upper-limb FET (i.e. voluntary exercise supplemented by peripheral electrical stimulation) might also induce increase in cortical excitability. The objective of the present study was to investigate if a single session of FET for finger flexion produces greater changes in cortical excitability than either voluntary exercise or peripheral ES alone.

2. METHODS

Eight subjects with no known history of neuromuscular disorder volunteered to participate in this study. All of the experiments were conducted in accordance with the Declaration of Helsinki. The experimental protocol was approved by the local ethical committee and all subjects gave their written informed consent prior to their participation.

The setup for upper-limb FET is fully described by Popovic *et al.* [3]. Clinically, upper-limb FET for grasp function is conducted with a four-channel stimulator programmed to control hand opening and closing (finger flexion/extension and thumb abduction/adduction). In this study, we used a reduced version of FET where the stimulation was restricted to finger flexion/extension alone. The excitability of the finger flexor area in the motor cortex was examined after 20 minutes of training.

2.1. Electrical Muscle Stimulation

The stimulation was applied using disposable self-adhesive surface electrodes with the cathodes positioned over the respective motor points of the flexor muscles (Flexor Digitorum Profundus (FDP) and Flexor Digitorum Superficialis (FDS)) and the Extensor Digitorum Communis (EDC). A common anode was placed on the lateral surface of the forearm just proximal to the wrist. The electrode positions were carefully selected to ensure that the opening and closing movements of the hand were as natural as possible. The stimulation pattern was designed to mimic the activity of fingers that is typical of slow grasping and releasing. The pulse duration, frequency, and amplitude (current) were set to minimize discomfort during stimulation yet produce a finger flexion/extension movement that would allow the subject to grasp and lift a 50 cl bottle of water without voluntary assistance (e.g.: f=50 Hz, T=200 µs, I=6–13 mA.

2.2. Transcranial Magnetic Simulation

Transcranial magnetic stimuli (Magstim Rapid^2, Magstim Company, Dyfed, UK) were used to evaluate cortical excitability before and after each training session. Motor evoked potentials (MEPs) were elicited by applying magnetic stimuli with a custom-made 90 mm double coil (batwing design; type no. 15411, Magstim company, Dyfed, UK) to the left hemisphere (contralateral) motor cortical finger area at the hot spot for activation of the finger flexor muscles (FDP and FDS). The subject's head was fixed with a padded support and the coil was secured to ensure that the same area of the cortex was stimulated throughout the experiment.

2.3. Peripheral Nerve Simulation

Peripheral nerve stimulation was used to normalize the magnetic evoked potentials so that intra-subject comparisons could be made between MEPs measured during different test sessions. A compound action potential in the finger flexors was elicited with monopolar electrical stimulation of the median nerve. The EMG responses representing the direct motor stimulation (M-wave) were monitored as the stimulation intensity was increased from a subliminal level until there was no further increase in the peak-to-peak amplitude of the M-wave with increasing intensity. The stimulation amplitude was then increased by approximately 15%. This supra-maximal stimulation level was used to elicit the maximal M-wave (M_{max}) to which the MEPs were normalized.

2.4. Experimental Protocol

Each subject participated in three training sessions involving 20 minutes of hand grasp exercise where they lifted a 50 cl water bottle. The three training sessions involved FET, ES alone, and VOL alone. The experiments were conducted in three different sessions with at least 24 hours between each session.

A stimulus-response input-output curve was constructed before and after each training session by measuring MEPs with a series of single pulse magnetic stimuli delivered at a random inter-stimulus interval of 1-1.5 s and pseudo-random stimulus intensity. The MEPs were quantified as the peak-to-peak amplitude, and expressed as a percentage of the M_{max}. The normalized MEPs were then plotted against the stimulus intensity.

2.5. Analysis

Data analysis was conducted offline. The normalized stimulus-response input-output curve data were modeled with a three-parameter sigmoid equation:

$$y = \frac{a}{1 + e^{-(x-x_0)/b}}$$

where a, b and x_0, describe the height, slope, and center point of the curve, respectively. The parameters were estimated by fitting this equation to the MEP data with a Marquardt-Levenberg nonlinear least squares algorithm. The percent change from the pre-training to post-training was calculated for each parameter. A one-way repeated measures ANOVA was used to test for statistically significant differences as a result of training and a Scheffé multiple-comparison test was used to test for difference between training conditions. All statistical tests were conducted with a significance level of 0.05.

3. RESULTS

A set of stimulus-response input-output curves for a single subject is illustrated in Figure 1A-C. For the FET condition, the maximum height of the curve is increased and there is a clear left-shift with respect to the pre-training curve. In contrast, there is only a small change in the ES curve and no change in VOL. In this case, parameter a increased by 127%, 24% and 6% for FET, ES and VOL respectively. Across all subjects, only parameter a showed a significant increase with training (a: P=0.001; b: P=0.88; x_0: P=0.94). The results for parameter a are illustrated in Figure 1D. Training for 20 min produced a change in parameter a of 83%, -1.5%, and 1% for FET, ES, and VOL, respectively. The Scheffé multiple-comparison post-hoc test indicated that the FET group was significantly different from the ES and VOL groups (P<0.05).

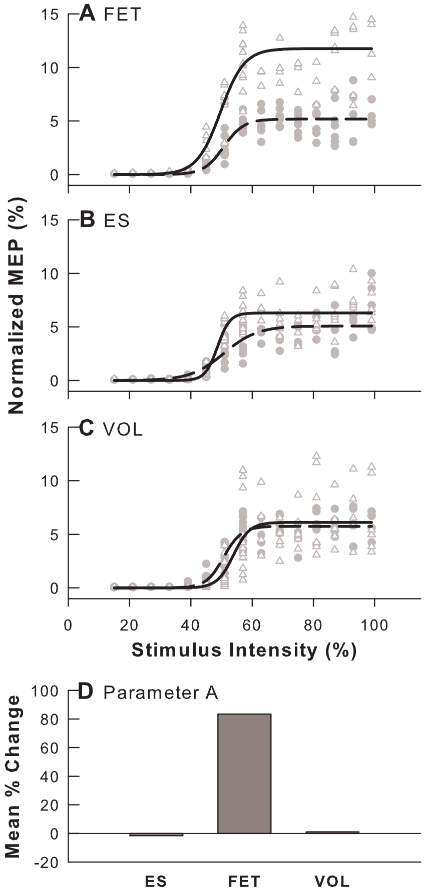

Figure 1. A-C) Stimulus-response input-output curves for finger flexor MEPs normalized to M_{max}. Responses after training (solid lines) are shown superimposed on pre-training curves (dashed lines). D) Mean percent change in parameter *a* (input-output curve maximum) across all subjects.

4. DISCUSSION AND CONCLUSIONS

A single session of FET training for 20 min in healthy subjects produced changes in TMS-assessed cortical excitability. This observation provides evidence for the suggestion that one of the methods by which FET enhances motor recover following stroke is to increase cortical plasticity. For the upper limb this phenomenon seems to be significantly greater for FET than either ES or voluntary exercise applied alone. However, it is surprising that no significant changes were found with either the ES or VOL conditions alone. Based on these results more investigation into the effects of FET on cortical excitability is warranted to improve its effectiveness in acute post-stroke rehabilitation.

References

[1] Popovic,D.B., Popovic,M.B., Sinkjaer,T., Stefanovic,A., Schwirtlich,L., Therapy of paretic arm in hemiplegic subjects augmented with a neural prosthesis: a cross-over study, Can. J. Physiol Pharmacol., 82 (2004) 749-756.

[2] Gritsenko V., Prochazka A., A functional electric stimulation-assisted excersise therapy system for hemiplegic hand function, Arch. Phys. Med. Rehabil. 85 (2004) 881-885.

[3] Popovic,M.B., Popovic,D.B., Sinkjaer,T., Stefanovic,A., Schwirtlich,L., Clinical evaluation of Functional Electrical Therapy in acute hemiplegic subjects, J. Rehabil. Res. Dev., 40 (2003) 443-453.

[4] Karni,A., Meyer,G., Jezzard,P., Adams,M.M., Turner,R., Ungerleider,L.G., Functional MRI evidence for adult motor cortex plasticity during motor skill learning, Nature, 377 (1995) 155-158.

[5] Ridding,M.C., McKay,D.R., Thompson,P.D., Miles,T.S., Changes in corticomotor representations induced by prolonged peripheral nerve stimulation in humans, Clin. Neurophysiol., 112 (2001) 1461-1469.

[6] Khaslavskaia,S., Sinkjaer,T., Motor cortex excitability following repetitive electrical stimulation of the common peroneal nerve depends on the voluntary drive, Exp. Brain Res., (2005).

[7] Kido,T.A., Stein,R.B., Short-term effects of functional electrical stimulation on motor-evoked potentials in ankle flexor and extensor muscles, Exp. Brain Res., 159 (2004) 491-500.

[8] Knash,M.E., Kido,A., Gorassini,M., Chan,K.M., Stein,R.B., Electrical stimulation of the human common peroneal nerve elicits lasting facilitation of cortical motor-evoked potentials, Exp. Brain Res., 153 (2003) 366-377.

Acknowledgements

This study was funded by grants from the Danish National Research Council and Det Obelske Familiefond.