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Original Article

Effects of the combination therapy of tilt sensor functional electrical stimulation and integrated volitional control electrical stimulation on brain activity during the subacute phase following stroke: a feasibility study

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Abstract. [Purpose] The aim of this study was to investigate whether the combination of integrated volitional control functional electrical stimulation and tilt sensor functional electrical stimulation training affected brain activation during the subacute phase following a stroke. [Participant and Methods] The patient was a 60-year-old male with right hemiparesis, secondary to stroke in the left thalamus. Conventional intervention was performed for 60 minutes per day during the first two weeks of treatment (the control condition). Functional electrical stimulation intervention, including integrated volitional control functional electrical stimulation and tilt sensor functional electrical stimulation training, was then performed for 60 minutes per day for two weeks (the experimental condition). These sessions were repeated four times. Brain activity was measured during voluntary right ankle dorsiflexion in both sessions, using functional magnetic resonance imaging. Brain activity measurements were obtained a total of eight times every two weeks (34, 48, 62, 76, 90, 104, 118, and 132 days following the stroke). [Results] There was a significantly higher level of activation in the bilateral cerebellum and the left side of the supplementary motor area in the experimental condition than in the control condition. [Conclusion] The present study demonstrates that the combination of integrated volitional control functional.

Key words: Integrated volitional control FES, Tilt sensor FES, Brain activity

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INTRODUCTION

Among various FES devices, an integrated volitional control FES and a tilt sensor FES are reported as effective clinical interventions for individuals experiencing walking difficulties due to foot drop. The integrated volitional control FES training over the tibialis anterior muscle enhances the patient's voluntary ankle dorsiflexion by detecting volitional electromyography (EMG) signals during the muscle activity[1)]. This training improved motor function of chronic stroke patients[2)]. However,

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it is necessary to perform not only ankle dorsiflexion training, but also actual walking practice to improve walking ability for daily living. On the other hand, the tilt sensor FES stimulates the tibialis anterior to improve foot clearance during the swing phase of gait. Research in neurological diseases reported that the tilt sensor FES training helped increase the range of ankle dorsiflexion in the initial floor contact[3], which seems to improve the walking speed and activities of daily living[4]. The mechanism of FES during walking is based on movement prediction and sense of agency/body ownership[5]. Therefore, the combination of integrated volitional control FES and tilt sensor FES trainings may lead to functional alteration of brain activities.

The purpose of this study was to investigate whether gait training with the tilt sensor FES after movement training of ankle dorsiflexion with the integrated volitional control FES affected brain activation in a post-stoke patient.

PARTICIPANT AND METHODS

The patient was a 60-year-old man (height=167.2 cm, weight=62.0 kg) who had right hemiparesis due to a brain hemorrhage in the left thalamus. The lesion was situated in the posterior limb of internal capsule and a part of basal ganglia. The size of ecchymoma was 29.5 mm × 19.7 mm × 24.7 mm confirmed by a computed tomography scan. The patient started standard inpatient rehabilitation two days after the stroke onset. The patient showed difficulty with dorsiflexion of the ankle joint, which made many activities of daily living (ADL) difficult. Scores of functional independences measure (FIM) was 67 points. Moreover, he exhibited lower extremity spasticity and was unable to perform voluntary ankle dorsiflexion beyond 0 degrees. No cognitive impairment was noted. After obtaining an approval by the local ethics committee, the patient provided written, informed consent. The study was registered with the Shiroishi Kyoritsu Hospital (trial registration number 20160).

Physical therapy including conventional intervention was performed for 60 minutes per day, during the first two weeks (the control condition; CON), and then completed the FES intervention for 60 minutes every day following two weeks (the experimental condition; FES). Those sessions were repeated four times (CON 1, FES 1, CON 2, FES 2, CON 3, FES 3, CON 4, and FES 4 conditions). FES devices were applied to perform the integrated volitional control FES training using IVES (OG Giken, Okayama, Japan), and the tilt sensor FES training using WalkAide (Innovative Neurotronics, Austin, TX, USA). The integrated volitional control FES system was composed of three conductive gel surface electrodes: two recording electrodes and one ground electrode. To maximize ankle dorsiflexion, electromyography-triggered neuromuscular electrical stimulation provides preset electrical stimulation when the tibialis anterior muscle activity during voluntary ankle dorsiflexion reaches a target threshold. For the present study, the device driver was set to a maximum of 300 μs pulse and frequency to a maximum of 20 Hz., and voluntary ankle dorsiflexion was repeated for 30 minutes. The tilt sensor FES device was used to deliver asymmetrical biphasic surface electrical stimulation to the common peroneal nerve, triggered by an individually programmed tilt sensor. The device driver was set to a maximum of 300 μs pulse and frequency to a maximum of 33 Hz. Software provided the WalkAide device with the timing of electrical stimulations to facilitate his ankle dorsiflexion during the swing phase of walking. The gait training with WalkAide device was performed for 30 minutes.

The primary physical outcome measures were walking speed using a 10-meter walking test (10MWT), which was used to evaluate gait performance. There were two secondary outcome measures; the Fugl-Meyer assessment (FMA) to evaluate lower extremity impairment[6], and the modified ashworth scale (MAS) to assess muscular tone for ankle joint[7]. These outcome measures were obtained a total of eight times at pre- and post-intervention every 2 weeks (34, 48, 62, 76, 90, 104, 118, and 132 days since post-stroke).

FMRI is non-invasive and has relatively high spatial resolution with regarding to movement from one part of the limbs. FMRI has established the mechanism showing a positive relationship between intensity of physical function and cortical activation measured by the blood oxygenation level-dependent (BOLD) response. MRI data were collected with a 1.5 T Nova Dual (Philips, Amsterdam, The Netherlands). FMRI were acquired with echo-planar imaging (EPI) for obtaining the functional images as follows: repetition time (TR)=3,000 ms; echo time (TE)=50 ms; matrix 64 × 64; field of view (FOV)=230 × 230 mm; voxel size=3.59 × 3.59 × 4.00 mm; 36 axial slices. The T1-weighted anatomical images were acquired as follows: TR=930 ms; TE=7.6 ms; T1=993.7 ms; flip angle=10 degrees; 160 slices; matrix 256 × 256; FOV=230 × 230 mm.

During the fMRI assessments, the patient rested comfortably in a supine position on a bed in the MRI room. His head was immobilized by cushions. This study used a blocked design consisting of four task-rest blocks. In each task, the patient performed voluntary right ankle dorsiflexion of paretic side. The motor paradigm consisted of 30-second periods of task followed by 30-seconds of rest first for the right ankle. The patient was instructed to avoid body movements except his right foot.

Image processing and statistical analyses were performed using a Statistical Parametric Mapping software (SPM12) (Welcome Department of Cognitive Neurology, London, UK) package implemented in Matlab 2015a (Math Works, Inc., Natick, MA, USA). To investigate the main effects of each task, one-sample t-tests were conducted using appropriate contrast images. Two-sample t-tests using appropriate contrast images for each task were performed to examine the differences between the FES and control conditions. The significance level set to $p<0.001$ for multiple comparisons within specific regions of interest (ROIs). Our predefined area of investigation included the following; sensorimotor region, and cerebellum area.

RESULTS

At average, the patient performed 344.4 counts/day of repetitive right ankle dorsiflexion using IVES during the FES 1 condition. The patient performed 434.3 counts/day using IVES, and 468.6 meter/day for gait training using WalkAide during the FES 2 condition. Patient performed 500.0 counts/day using IVES, and 623.6 meter/day using WalkAide during the FES 3 condition. The patient performed 500.0 counts/day using IVES, and 944.3 meter/day using WalkAide during the FES 4 condition. The 10MWT time was continuously decreased after every two weeks (48, 62, 76, 90, 104, 118, and 132 days since post-stroke) (Table 1). Regarding the average values of physical functions, 10MWT time was decreased after the experimental condition compared to the control condition (the control condition; 0.11 ± 0.05 m/s, the experimental condition; 0.25 ± 0.13 m/s).

Both the control and the experimental conditions significantly increased the BOLD signals of several brain regions with voluntary ankle dorsiflexion compared to the resting. In addition, the bilateral cerebellums and contralateral side of the supplementary motor area (SMA) significantly increased BOLD signals of the experimental condition as compared to that of the control condition (Fig. 1).

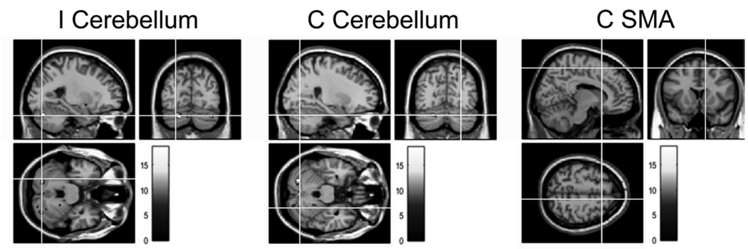
DISCUSSION

The purpose of this case study was to investigate whether the combination of integrated volitional control FES and tilt sensor FES trainings affect brain activity. We found that the 10MWT were improved after the experimental condition compared to the control condition. Muscle activity of the tibialis anterior is required for the swing phase as well as the initial contact within the stance phase to smoothly move in a gait cycle. In the swing phase, the tibialis anterior muscle maintains the

Table 1. Changes in physical outcome measures in both the control and the experimental conditions

	CON 1	FES 1	CON 2	FES 2	CON 3	FES 3	CON 4	FES 4
Time since stroke (days)	34	48	62	76	90	104	118	132
10MWT (m/s)								
T-cane	0.16	0.53	0.65					
Without support			0.56	0.82	0.87	0.94	1.09	1.40
FMA-LE (points)	23	26	27	29	30	30	30	31
MAS (points)	1+	1	2	1+	2	2	2	2

CON: control condition; FES: functional electrical stimulation condition (experimental condition); 10MWT: 10-meter walking test; FMA-LE: Fugl-Meyer assessment for lower extremity; MAS: modified Ashworth scale.



Location	Side	MNI coordinates x	y	z	Peak voxel T-value	Z-value
FES > Control						
Cerebellum	I	-24	-74	-26	17.53	4.73
	C	26	-70	-26	7.61	3.64
Supplementary motor cortex	C	10	16	62	5.31	3.12

I: ipsilateral side; C: contralateral side; SMA: supplementary motor cortex;
MNI: montreal neurological institute.
Significant activation at uncorrected p<0.001.

Fig. 1. Brain activity regions during voluntary ankle dorsiflexion for each task were performed to examine the differences between the FES and control conditions. The bilateral cerebellums and contralateral side of the SMA significantly increased BOLD signals of the FES condition as compared to the control condition.

appropriate distance between the floor and the foot, and at the initial contact, it controls the eccentric contraction in the ankle rocker[8]. The common key mechanism of both integrated volitional control FES and tilt sensor FES devices is to facilitate the motor function of the tibialis anterior muscle. Given that repetitive voluntary ankle dorsiflexion and walking training focused on swing phase improved gait performance, it's possible that integrated volitional control FES and/or tilt sensor FES trainings helped to improve the walking speed.

We evaluated not only walking ability but also brain activities during ankle dorsiflexion using fMRI. BOLD signals in the contralateral SMA and cerebellum were significantly increased after FES training as compared to the control condition. A previous fMRI study demonstrated that SMA was related to movement preparation and planning[9], and stroke patients' response in the SMA was increased by the carryover effect of the FES[5]. The activation of cerebellum increased during the motor skill learning[10]. This region modulates the errors between intended motor prediction and the actual motor behavior. An appropriate voluntary movement leads to the feedback-error learning by repeating the training[11]. Thus, the previous study reported that changes in SMA and cerebellum connectivity might occur to compensate for a dysfunctional primary motor cortex in stroke patients[12]. In the present study, combined FES training might play an important role in the motor recovery due to SMA and cerebellum re-connectivity.

During the acute stroke phase, behavioral recovery was correlated with increased brain activities in the primary motor cortex, premotor cortex, and supplementary motor cortex[13]. Although it is well reported that stroke patients with a moderate to severe motor dysfunction improve health-related functional status by early rehabilitation[14]; effects of FES intervention on subacute post-stroke patients' physical function and brain activity is unknown. The post-stroke patients in a subacute phase show significant improvement of physical function during hospitalization by rehabilitation[15]; therefore, it is crucial to assess effects of rehabilitation including FES intervention by objective measurement such as fMRI.

The present study has a few limitations. First, it was optimal to include the FES condition with only integrated volitional control FES or tilt sensor FES training. It is difficult to evaluate determine whether a combination of integrated volitional control FES and tilt sensor FES trainings affects more the brain activities and physical function compared to integrated volitional control FES only or tilt sensor FES training only. Second, this case study included a possibility of potential natural recovery due to subacute stroke. Despite these limitations, the present study is the first to describe how this training supports the neurophysiological alteration in subacute stroke. We observed short-term changes in brain activity after hybrid FES training, suggesting motor relearning in response to the activation of feedback pathways. The combination of integrated volitional control FES and tilt sensor FES trainings seems to facilitate both motor recovery related to the brain regions and improvement of gait performance.

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Conflict of interest

There are no conflicts of interest.

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