Effect of electrical stimulation therapy on upper extremity functional recovery and cerebral cortical changes in patients with chronic hemiplegia

Kana SASAKI1, Toshiki MATSUNAGA2, Takenori TOMITE1, Takayuki YOSHIKAWA1, and Yoichi SHIMADA1
1Department of Orthopedic Surgery, Akita University Graduate School of Medicine and 2Department of Rehabilitation Medicine, Akita University Hospital, Akita 010-8543, Japan
(Received 8 December 2011; and accepted 26 December 2011)

ABSTRACT
Hemiplegia is a common sequel of stroke and assisted living care is needed in many cases. The purpose of this study was to evaluate the effect of using surface electrode stimulation device in rehabilitation, in terms of functional improvement in upper limb and the changes in brain activation related to central nervous system reconstruction. Five patients with chronic hemiplegia received electrical stimulation therapy using the orthosis-type surface electrode stimulation device for 12 weeks. Training time was 30 min/day for the first weeks, and increased 30 min/day in every 4 weeks. Upper limb outcome measures included Brunnstrom stage, range of motion, Fugl-Meyer assessment and manual function test. Brain activation was measured using functional MRI. After therapy with therapeutic electrical stimulation (TES) for 12 weeks upper limb function improved in all cases. The results of brain activation showed two patterns. In the first, the stimulation produced an activity in the bilateral somatosensory cortices (SMC), which was seen to continue over time. The second, activation was bilateral and extensive before stimulation, but localized to the SMC after intervention. Treatment with TES using an orthosis-type electrode stimulation device improves upper limb function in chronic hemiplegia patients. The present findings suggest that there are not only efferent but also afferent effects that may promote central nervous system remodeling.

Stroke is the main cause of disability in industrialized countries, with a significant impact on individual, family, and societal healthcare. Although many hemiplegic survivors after stroke achieve independent ambulatory functions with orthotic devices, half of them are unable to use their upper extremity in their activities of daily living (ADL) after months of standard stroke rehabilitation (31). A common approach in rehabilitation for upper limb hemiplegia in chronic stage has been training the healthy side, especially if it contains the nondominant hand, and learning to perform tasks with only one arm. In recent years, it has been recognized that the phenomenon of “learned non-use” (30, 33), which results from use of the healthy side only, invites a state of further inability to use the affected side. Because this can lead to exacerbation of secondary disorders such as edema, pain, decreased range of motion, and shoulder subluxation, attention has focused on approaches for rehabilitating the affected upper limb based on the plasticity of the central nervous system. Reports that rehabilitation for the affected upper limb produces reconstruction of the central nervous system as upper limb function improves (27) have also attracted attention.

One of the most promising alternate interventions to help hemiplegic survivors recover upper limb function is functional electrical stimulation (FES). FES is a method of restoring function to upper or lower extremities by electrically stimulating the lower motor neurons of hemiplegic survivors after stroke (26). FES training involves the effect of ther-
apeutic electrical stimulation (TES) for the paralyzed muscles. These techniques are both used on the affected upper limb and are effective in improving muscle atrophy or limited range of motion in joints from paralysis following stroke. The primary focus of FES development was to produce assistive devices that could be worn or implanted and used in ADLs (19, 26). More recently, evidence has emerged that FES can be applied as part of a clinical intervention for training. It has been reported that people who use FES to activate paretic muscles on a regular basis sometimes improve their voluntary control of those muscles, that is without FES (12, 25). Popovic and colleagues called this “FES therapy” (23).

Preprogrammed FES systems designed to assist stroke patients to perform selected upper extremity daily functions are uncommon in clinical practice (7). A small number of FES devices have been tested as interventions for chronic stroke (4). The NESS H200™ is a new multichannel neuroprosthesis worn by the patient. This hybrid orthosis with built-in electrodes has been developed specifically to stimulate the extensor and flexor muscles of the paretic forearm as well as the thenar muscles of the hand in patients with enteral neurological disorders. There are some clinical reports of the effectiveness of this device for the hemiplegic survivors in chronic stage (2–4, 9, 24), however, the mechanisms of functional recovery after FES therapy is still unknown.

The purpose of this study was to evaluate the effect of using this surface electrode stimulation device in upper limb rehabilitation, in terms of functional improvement and reconstruction of paralyzed limbs and the changes in brain activation related to central nervous system reconstruction.

MATERIALS AND METHODS

Subjects. The subjects were patients with chronic hemiplegia and Brunnstrom stage 3–4 status more than 1 year after a stroke. Patients with an implanted pacemaker for use with an electrical stimulation device were excluded. Patients with skin disorder of the forearm or hand and patients with secondary neuronal disorder complications were also excluded from the analysis. In the end, the subjects comprised five patients (three men, two women) with a mean age of 69 years (range, 43–78 years). The mean time from occurrence of cerebral infarction was 2 years 8 months (range, 13 months to 7 years 10 months). In all cases, the patient had reached a plateau in the recovery of neurological upper limb function. The affected side was the right side in three patients and the left side in two patients. In all five patients, control of the primary disease and general condition were good, and these patients understood and were motivated for therapy. A full explanation was given to the patients before the start of therapy and informed consent was obtained.

Training. Electrical stimulation was given once a day using the NESS H200™ orthosis-type electrode stimulation device (Bioness Inc., Valencia, CA) and continued for 12 weeks. The training consisted of repeated finger extension and flexion movement from the electrical stimulation. At the first week, training time was set for a 30 min/day, considering muscle fatigue in patients with chronic hemiplegia, then increased 30 min/day in every 4 weeks. The NESS H200™ device consists of a small control unit and a lightweight orthosis that fits on the forearm. Its operation is very simple and can be performed by the patient himself or herself. There are five stimulation electrodes that are embedded in advance to stimulate the common digital extensor muscle, extensor pollicis brevis or longus muscle, thenar muscle, flexor digitorum superficialis muscle, and flexor pollicis longus muscle. Once the electrode positions are determined at the initial fitting, the same response can be obtained every time by simply putting on the orthosis and selecting the mode of use. The frequency used is either 18 Hz or 36 Hz, depending on the movement.

Outcome measures. Measurements of upper limb function included Brunnstrom stage (arm, fingers), grip strength, passive range of motion [thumb metacarpophalangeal joint (MPJ) extension and flexion], total motion in fourth finger flexion [total of MPJ + proximal interphalangeal joint (PIP) + distal interphalangeal joint (DIP)], Fugl-Meyer Assessment (FMA) (upper limb function) (10), and manual function test (21, 22). Evaluations were done before the start of therapy and 4, 8, and 12 weeks after the start of therapy. ANOVA (Stat-View version 5, Cary, NC, USA) was used to statistically analyze differences in the percentage of improving rate after TES.

Brain activation was measured using functional MRI a total of four times: before the start of therapy and 4, 8, and 12 weeks after the start of therapy. The MRI scanner used was a 1.5-T clinical use scanner made by GE Healthcare (Signa EXCITE). The task during imaging was an active gripping movement, with rest and the task movement repeated at 30-sec intervals. Rest-task movement was tak-
Effect of ES therapy for chronic hemiplegia

RESULTS
Upper limb function improved in all cases after therapy with TES for 12 weeks. Brunnstrom stage increased in arms from 4.2 ± 0.4 (mean ± SD) before therapy to 4.8 ± 0.4 after therapy for 12 weeks (Fig. 1-1) and in fingers from 4.8 ± 0.4 before therapy to 5.6 ± 0.49 after therapy for 12 weeks (Fig. 1-2).

Grip strength rose slightly from 11.2 ± 5.35 kg before therapy to 11.9 ± 4.96 kg at 12 weeks. Range of motion for the thumb MPJ increased in extension from 5° ± 4.47° before therapy to 12° ± 2.45° at 12 weeks (Fig. 2-1) and in flexion from 51.2° ± 11.27° before therapy to 59.4° ± 0.8° at 12 weeks (Fig. 2-2). Range of motion for the second finger increased from 239° ± 28.71° before therapy to 259° ± 12.81° at 12 weeks (Fig. 2-3) and range of motion for the fourth finger increased from 252.8° ± 31.77° before therapy to 264.8° ± 15.43° at 12 weeks (Fig. 2-4). Improvements in these functions were obtained at 4 weeks after the start of therapy and the effect tended to be maintained until the conclusion of therapy at 12 weeks.

FMA of upper limb function improved from 41.8 ± 5.08 to 51.6 ± 5.28, and there was a tendency for this to increase every 4 weeks during therapy (Fig. 1-3). Using analysis of variance to examine the improvement rates every four weeks after stimulation, it was found that FMA upper limb function improved significantly with time (ANOVA, P = 0.019) (Fig. 3).

Similar results were obtained with the manual function test, which increased from 18.2 ± 4.17 before therapy to 22.4 ± 3.93 at 12 weeks (Fig. 1-4). Particularly good improvement was obtained in the tasks of carrying cubes, from 3.6 ± 2.06 cubes before therapy to 4.8 ± 1.47 cubes at 12 weeks, and the pegboard test, from 4 ± 2.45 pegs before therapy to 5.8 ± 2.93 pegs at 12 weeks.

The results of fMRI showed two patterns of brain activation. In the first, stimulation produced activity in the bilateral somatosensory cortices (SMC), which was seen to continue over time. Although activation

---

**Fig. 1-1** Brunnstrom stage (arms) pre and post TES (mean ± SD) (n = 5).
**Fig. 1-2** Brunnstrom stage (fingers) pre and post TES (mean ± SD) (n = 5).
**Fig. 1-3** Fugl-Meyer assessment of upper limb function finger pre and post TES (mean ± SD) (n = 5).
**Fig. 1-4** Manual function test pre and post TES (mean ± SD) (n = 5).
DISCUSSION

In recent years, various therapies for upper limb dysfunction have been reported, and improvements in upper limb function are also expected in the chronic phase. In addition to the therapeutic electrical stimulation used in the present study, therapeutic approaches for upper limb dysfunction on the affected side include constraint-induced movement therapy (29, 33, 34), repetitive transcranial magnetic stimulation (rTMS) (14, 15, 28), orthotic therapy (11, 13, 32), and robot therapy (17, 20). While positive results have been reported with all of these therapies, the number of reports is small, and consensus has not been reached on methods, duration, or frequency.

Alone et al. continued electrical stimulation therapy 2–3 times/day for 5 weeks in 77 patients with chronic hemiplegia, and they reported improved upper limb function, diminished spasticity, and reduced pain (4). In the present study with therapeutic electrical stimulation (TES) once/day for 12 weeks, patients who had reached a temporary plateau in the recovery of neurological upper limb function showed improved upper limb function, with significant im-

was seen in the bilateral SMC in all cases with this pattern, the activation was stronger on the involved side (Fig. 4). The second pattern was bilateral, extensive activation before stimulation, but localized to the SMC after intervention (Fig. 5).

In cases when changes in brain activation occurred, the changes began four weeks after electrical stimulation.
provement in FM scores as the period of treatment increased. The above suggests that electrical stimulation therapy is effective for improving upper limb function of patients with chronic hemiplegia. The mechanisms for improvement in upper limb function are thought to include elimination of learned non-use on the part of the patient, functional remodeling of the central nervous system from an afferent effect of electrical stimulation, and reduced spasticity from improved reciprocal inhibition at the spinal cord level.

In investigations with fMRI during one-hand movements following stroke, activation of not only the contralateral SMC but also the ipsilateral SMC was seen in the past, and there have been reports of broad activation of surrounding areas of cerebral cortex, such as the supplementary motor area (SMA) and premotor cortex (PMC), with even simple repetitive movements. With regard to functional recovery of the upper limbs, Cramer et al. (8) and Cao et al. (5) reported that chronic hemiplegia patients with good recovery had increased activation of the SMC of the ipsilateral hemisphere (uninvolved side) compared with control groups. Reported evaluations following rehabilitation intervention include a study by Marshall et al., who reported that, during movement of the affected arm, the ratio of contralateral activation to ipsilateral activation increased with time. They suggested that the importance of the contralateral SMC (involved side) increases with recovery (18). Carey et al. evaluated brain activation and task accuracy before and after training in chronic hemiplegia patients, and they found that, together with improvement in accuracy of trained tasks, SMC and PMC activation changed from uninvolved hemisphere to involved hemisphere dominance (6). These and other reports on remodeling of the central nervous system have attracted attention, but there have been few investigations of changes in brain activation before and after intervention with electrical stimulation.

Kimberly et al. applied electrical stimulation for
involved side. From this and past reports it appears that a certain level of remodeling occurs in the central nervous system starting before electrical stimulation intervention. The pattern in which post-stimulation brain activation is concentrated in the SMCs does not contradict past reports, and it is possible that there was remodeling of the cerebral cortex involved in voluntary movement. This suggests the possibility that treatment with TES is effective in not only improving efferent upper limb function, but it also acts afferently and contributes to central nervous system remodeling. However, the site and extent of brain activation is also affected by individual differences, including the location and severity of the damaged area, dominant hand, and degree of paralysis. Further investigation with a larger number of patients is planned.

The number of strokes is increasing annually, and to prevent and ameliorate secondary impairments from chronic hemiplegia, we should consider not only improvement of decreased function through 60 min over three days and reported that the index of cortical intensity in the SMC of the uninvolved side rose significantly after treatment (16). Shin et al. divided 14 stroke patients with chronic hemiplegia into an electrical stimulation group and a standard rehabilitation group, and they reported changes in upper limb function and brain activation following electrical stimulation 1 h/day, 5 days/week, for 10 weeks (27). According to their report, however, SMC activity changed from the uninvolved to the involved side after rehabilitation intervention using TES, and this occurred along with improvement in purposeful function. In the present study, activity in the bilateral SMCs was seen before stimulation. There were two patterns, one in which this activation continued throughout the course, and one in which the activation was bilateral and extensive before stimulation, and then became localized in the SMCs after intervention. In patients with activation in bilateral SMCs before stimulation, the activation was stronger on the involved side than on the uninvolved side. From this and past reports it appears that a certain level of remodeling occurs in the central nervous system starting before electrical stimulation intervention. The pattern in which post-stimulation brain activation is concentrated in the SMCs does not contradict past reports, and it is possible that there was remodeling of the cerebral cortex involved in voluntary movement. This suggests the possibility that treatment with TES is effective in not only improving efferent upper limb function, but it also acts afferently and contributes to central nervous system remodeling. However, the site and extent of brain activation is also affected by individual differences, including the location and severity of the damaged area, dominant hand, and degree of paralysis. Further investigation with a larger number of patients is planned.

The number of strokes is increasing annually, and to prevent and ameliorate secondary impairments from chronic hemiplegia, we should consider not only improvement of decreased function through

![Fig. 5 Changes of cerebral cortical activation 2: bilateral, extensive activation before stimulation, but localization to the SMC after intervention.](image-url)
compensation measures, such as changing the dominant hand, but also suitable approaches to upper limb dysfunction on the affected side. The orthosis-type electrode stimulation device (NESS H200™) used in this study has surface electrodes embedded in a plastic forearm orthosis. The electrodes are pad-type. If an appropriate response to stimulation is obtained at the first time fitting, TES and FES for contraction of paralyzed muscle can be done subsequently by simply putting the device on. This device makes it possible to conduct rehabilitation easily, efficiently, and effectively, and it can be operated by the patients themselves or family members. Many facilities are limited in their ability to implement the approaches described above, and continuation of treatment is difficult under current medical and insurance systems. However, the orthosis-type electrode stimulation device (NESS H200™) is promising as a means of treatment that overcomes these difficulties. Moreover, since it provides not just simple electrical stimulation but can be used also for FES, training that uses patterns that are closer to actual ADL movements can be provided during TES. Thus, a functional training effect can also be obtained.

The present investigation was done with chronic hemiplegia patients as subjects, but a comparative investigation of upper limb functional assessments and changes in brain activation with a subject group that undergoes standard rehabilitation is needed. In addition, upper limb function and brain activation were investigated during the training period in this study, but an investigation of functional maintenance from a carry-over effect is also needed to judge the effectiveness of electrical stimulation. This is an issue for further study.

In conclusion, treatment with therapeutic electrical stimulation using an orthosis-type electrode stimulation device improves upper limb function in chronic hemiplegia patients. The present findings suggest that there are not only efferent but also afferent effects that may promote central nervous system remodeling.

REFERENCES


