Functional electrical stimulation-induced neural changes and recovery after stroke

H. WEINGARDEN 1, H. RING 2

Rehabilitation as a treatment approach to affect neural remodeling or “plasticity” of the injured brain is gaining increasing attention and appreciation. While rehabilitation continues to emphasize re-establishment of functional abilities, the approach of neurorehabilitation attempts to improve recovery by impacting on changes within the central nervous system rather than reliance on compensatory techniques. Functional electrical stimulation is one of the prominent modalities being used for neurorehabilitation. This report provides an overview of the relevance of brain plasticity to rehabilitation, and of the physiological and clinical studies that indicate the effects of functional electrical stimulation as a potential tool in neural remodeling.

Key words: Therapy, electric stimulation - Neuronal plasticity - Cerebrovascular accident - Hemiplegia - Rehabilitation.

Rehabilitation following hemiplegic stroke has typically emphasized re-establishment of function in mobility and activities of daily living, often based on the training of patients in compensatory strategies. The neurological deficits and potential for recovery have often been considered as issues for self-healing of those neural elements suffering only partial injury, and not significantly affected by physical treatments. However, an ever expanding body of basic science and clinical research now strongly demonstrate that these beliefs are no longer tenable. The intensive use of functional electrical stimulation (FES), a rehabilitation treatment modality, has been able to enhance the neurological outcome as compared to standard rehabilitation therapy.1, 2

Brain plasticity and rehabilitation - historical review

Nearly 25 years ago, Bach-y-Rita summarized the potential for new approaches in rehabilitation based upon laboratory studies of brain plasticity.3 He described two major physiological mechanisms underlying brain reorganization; unmasking of existing pathways for function, and sprouting of new connections. The first of these mechanisms may be thought of as relatively rapid, while the latter is a more gradual process occurring over a longer period of time. Basmajian (38th Annual John Stanley Coulter Lecture, American Congress of Rehabilitation Medicine, 1988) bemoaned

1 Sheba Medical Center Neurological Rehabilitation Department Department of Physical Medicine and Rehabilitation Sackler School of Medicine Tel Aviv University, Tel Aviv, Israel
2 Loewenstein Rehabilitation Hospital Neurological Rehabilitation Department Department of Physical Medicine and Rehabilitation Sackler School of Medicine Tel Aviv University, Tel Aviv, Israel

There was no funding or sponsorship for this paper.

Address reprint requests to: H. Weingarden, M.D., Neurological Rehabilitation Department, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel. E-mail: harold_h@netvision.net.il
the lack of progress in improving rehabilitation outcomes for stroke patients, and in particular the very limited recovery in the upper limb. He noted that inadequate demands upon the hemiplegic upper limb reinforced the problems of neglect, and caused what he described as a “psychosocial amputation”. He also discussed the “time locks” limiting the rehabilitation involvement to the early recovery phase after the cerebrovascular accident (CVA), and thus further limiting the potential for further recovery. In more recent times, the role of brain plasticity as a major factor in stroke recovery has become more widely accepted. The intensity of treatment has also been demonstrated to be a factor in brain reorganization. Despite these insights and challenges to the rehabilitation community, the actual changes in management have been driven by reimbursement issues. Duration of acute and rehabilitation hospitalization following stroke have decreased dramatically in the U.S. and other countries, but without a significant paradigm shift in treatment. Thus, the potential of improving the extent of functional recovery, or of lessening the physical impairments have remained unchanged.

**Brain plasticity and FES**

In the last several years, the promise of targeting brain plasticity in rehabilitation treatment for altering outcome has been actualized, and demonstrated to be a real factor for improving neurological impairments in both laboratory and clinical studies. In order to define brain remodeling involved in compensation for areas of brain injury, human clinical studies have utilized positron emission tomography (PET) scans, functional magnetic resonance imaging, focal magnetic stimulation, and high resolution electroencephalography (EEG), while dendritic volume, synaptic density, and intracellular recordings have been used in laboratory models. The presence of functional motor cortical reorganization has been shown after experimental CVA in primates. The authors found that representation may spread to areas of the brain previously uninvolved in the paretic movement, and originally activated for movement of other areas of the body. In addition, the loss of brain territory for a paretic movement enlarged when retraining was withheld, while this loss of adjacent territory was prevented by early retraining. The functional reorganization was accompanied by behavioral recovery. Studies in human stroke patients with recovered function have demonstrated increased regional cerebral blood flow to various regions of the brain when performing motor activities with their paretic hand. The areas include the ipsilateral sensorimotor cortex, the contralateral supplementary motor areas, insula, frontal operculum, and parietal cortex, areas not activated by motor activities of the intact hand. Recovery from internal capsule infarcts has been demonstrated to be associated with individually different patterns of functional reorganization of the brain. Prior to motor recovery, sensory input by means of passive movements has also been demonstrated to generate increased regional cerebral blood flow in patterns similar to those associated with substantial motor recovery.

A study using focal transcranial magnetic stimulation demonstrated rapid brain reorganization in response to electrical stimulation of a peripheral nerve. The study in human subjects without brain disorders measured the area of motor evoked potential (MEP) prior to and after nerve stimulation, and showed an increase in amplitude following the peripheral nerve stimulation. As the F-wave responses remained stable, the authors concluded that the peripheral stimulation caused a change in excitability of the primary cerebral cortex. In another study, pairing median nerve stimulation with transcranial magnetic stimulation induced increased amplitudes of motor responses in the APB. The plasticity evolved within 30 minutes, persisted for at least 30-60 minutes, and was topographically specific. An additional study showed differential inhibitory and facilitory effects on antagonist forearm muscles following 30 minutes of stimulation of the flexor carpi radialis (FCR). The MEP from the FCR was significantly reduced, while the MEP from the extensor carpi radialis was significantly enhanced, and there was no change in the MEP of the 1st dorsal interosseous. The specific molecular signal or signals to initiate functional reorganization of synaptic pathways has yet not been elucidated. There is evidence that neurotrophins may be a significant component of remodeling. Neurotrophins have been reported to increase after both peripheral nerve and brain injury, and are secreted in an activity-dependent manner. These trophic factors promote neuronal survival, and regulate synaptic transmission, stability, and efficiency at both developing and mature synapses. They have been identified as important for long-term potentiation,
and in the maturation of synapses. It has been suggested that functional electrical stimulation may cause central neurotrophic enhancement, thus promoting cell survival and axonal growth, permitting terminal synaptic connections, and facilitating synaptogenesis and neurogenesis. The repetitive activation of the anterior horn cell by means of retrograde conduction from the site of stimulation is certainly likely to generate the synaptogenic neurotrophins.

Reduction of spasticity from the use of functional electrical stimulation has been reported in a multitude of studies. Reciprocal inhibition, recurrent inhibition, and large sensory fiber activation have all been suggested as possible mechanisms for the spasticity reduction. Known neurophysiological pathways and empiric findings have been put forward to substantiate each of the mechanisms.

Studies on FES for the shoulder, especially with intensive use, have demonstrated improved outcomes of both the shoulder and the limb. Similarly, studies on the use of functional electrical stimulation for the more distal segments of the upper limb in stroke have nearly unanimously shown outcomes of improved active motion and strength as compared to control treatment.

In a crossover study comparing electrical stimulation to repetitive active hand movements, greater improvements were present in the active motion phase of treatment than in the electrical stimulation phase of treatment, other than a better spasticity reduction from the stimulation. However, the protocol called for the patients to actively inhibit any effort for voluntary movement during the stimulation, with the patients monitored with surface electromyography (EMG) to assure the lack of effort. This study in essence supports the concept of activity-derived neurotrophins being target and inhibitory/excitatory specific.

In a controlled study in chronic stroke patients of intensive use of electrical stimulation at home over a period of three weeks, the treated group had significant improvement in grasp and release hand tests, while the sham treatment group did not change. Furthermore, follow-up fMRI and a finger-tracking task, showed an index of cortical intensity in the ipsilateral somatosensory cortex increased significantly from pre-test to post-test following treatment. It was felt that these findings suggest that intensive FES may have an important role in stimulating cortical sensory areas allowing for improved motor function. The potential for improvements in upper limb functional tasks in patients with chronic severe hemiparesis by use of a neuroprosthesis treatment system has been demonstrated.

**Conclusions**

While the research and physiological basis for brain reorganization has been known to the rehabilitation community for decades, the establishment of routine treatment protocols based on these mechanisms has yet to occur. The basis of a brain plasticity approach to rehabilitation will include intensive treatment provided over longer durations that the usual rehabilitation hospitalization. FES fits as a prototype for this type of treatment, as it is efficacious in providing a high level of sensory-motor input into the central nervous system, and can potentially be used in an ongoing manner following the completion of the formal rehabilitation treatment program. Simplification of the application of FES by methods such as use of a neuroprosthesis may amplify the benefits by integrating the desired sensory-motor input with functional activities.

**References**