New trends in neurorehabilitation of subjects with central nervous system lesions

Novi trendi pri nevrorehabilitaciji oseb z okvaro centralnega živčnega sistema

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Abstract

Medical management and rehabilitation do not reverse paralysis, *i.e.*, alter the pathology and the impairment, but they have done much to improve the quality of life of persons with motor impairment by reducing their functional limitations. Rehabilitation technology requires a comprehensive approach that integrates the knowledge of physiology, psychology, biomechanics, engineering and physical and occupational therapy. In this review, the role of haptic robotics and electrical stimulation are presented with an emphasis on the future applications in clinics and possibly at home. More precisely, we present how the use of haptic robots that are assisting repetitive passive and active exercise contributes to the improvement of proximal joints (shoulder and elbow), while the use of functional electrical stimulation contributes to both proximal and distal joints of the paretic arm.

Izvleček

Zdravstvena obravnava in rehabilitacija sicer ne povrneta nastale paralize, tj. ne spremenita patologije in nezmožnosti živcev, vendar veliko prispevata k izboljšanju kakovosti življenja oseb z motoričnimi primanjkljaji s tem, da zmanjšata njihove funkcijske omejitve. Rehabilitacijska tehnologija zahteva celovit pristop, ki vključuje poznavanje fiziologije, psihologije, biomehanike, inženirstva in fizikalne ter delovne terapije. Članek prikazuje vlogo haptičnih robtov in elektrostimulacije s poudarkom na njihovi uporabi tako v kliničnih ustanovah kot na domu. Natančneje prikazuje, kako uporaba teh robotov, ki asistirajo pri ponavljajočih se pasivnih in aktivnih vajah, prispeva k izboljšanju stanja priležnih sklepov (ramena, komolci), medtem ko elektrostimulacija izboljša stanje tako priležnih kot tudi ostalih sklepov zgornjega uda s parezo.

Introduction

In this review, we will address two questions. First, why do we need improved rehabilitation for humans with upper limb disability (ULD)? Paralysis of the upper extremities is one of the most debilitating injuries that the body can experience following an injury of the central nervous system (CNS). Subjects with a CNS injury find themselves totally dependent on other people or devices for even the simplest tasks, which are normally taken for granted. Augmenting independence to a human with ULD will ultimately improve his/her quality of life. Second, how can we optimize the rehabilitation treatment in humans with ULD? Electrical activation of peripheral nerves is beneficial for their recovery; however, it cannot be easily implemented for proximal joints. Robotic assistance of movement is effective for recovery but is difficult to apply to assist grasping. Therefore, the aim is to integrate robotic and electrical stimulation treatments to achieve the highest degree of recovery of function for patients with ULD after stroke.

In providing some answers to the aforementioned questions, we present therapeutic methods and technologies that are emerging. Comprehensive conventional therapy[1] of subjects with ULD includes pharmacological means[2], enhanced physical therapy,[3,4] integrated behavioral therapy and physical therapy.[5-7] The common denominator of all these methods is that they allow

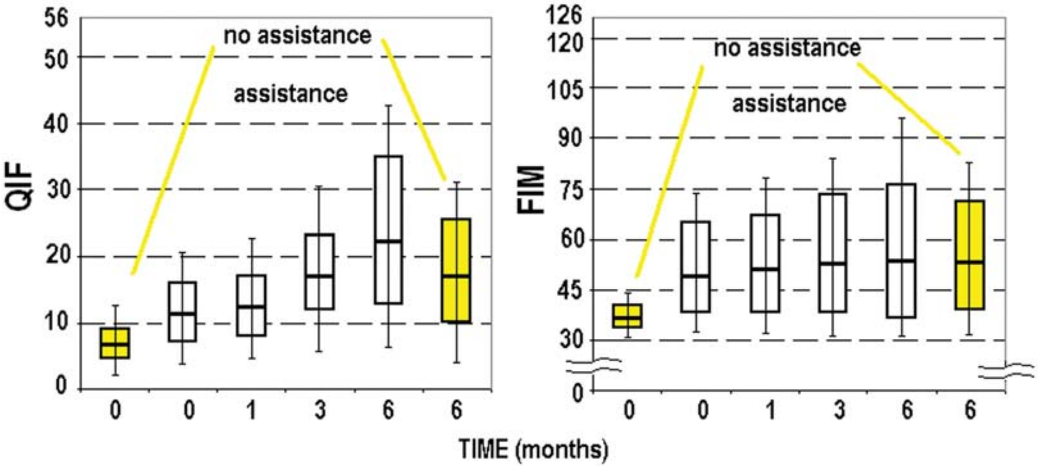

Figure 1: Quadriplegia index function (QIF, Max = 56) and functional independence measure (FIM, Max = 126) assessed before, during and after six months of using the Bionic glove or the Belgrade Grasping System in subjects with chronic tetraplegia.

intensive, task-oriented exercise with augmented feedback, thereby possibly contributing to better relearning as a consequence of increased cortical excitability.

Today, therapeutic strategies to promote recovery from stroke are utilizing the current knowledge of neural plasticity and the neuromodulatory role of physical rehabilitation. More precisely, current research interests are focused on adjuvant therapies that may enhance plasticity associated with recovery and rehabilitation.

We suggest that the timing and amount of the compensations of the missing motor functions provided by the assistant have major impact on the recovery. Compensatory processes relate to functional reorganization and/or functional adaptation. These processes are achieved by the reorganization of surviving neural circuits to enable a given behavior over circuits that are available. The major component of this mechanism is the therapy, or more precisely the training. Training leads to a redistribution of representations to non-damaged areas and partial restitution of the impaired neuropsychological processes on the basis of experience-dependent brain plasticity. Plastic reorganization follows two types of processes: 1) an alteration in synaptic sensitivity related to the unmasking of existing connections through changes in the inhibitory dynamics and 2) the reduced level of activity in the area of the lesion weakens the synaptic connections between the damaged and undamaged sites, leading to a reduction in the synchronous firing of cells in these two areas and thus weakening synaptic connectivity between them.

Electrical stimulation for therapy of subjects with ULD

We use two examples to illustrate the relearning and recovery caused by intensive exercise augmented by electrical stimulation over a prolonged period in subjects with tetraparesis and subjects with hemiparesis.

The first example comes from two clinical studies: 1) evaluation of the effects of use of the Bionic Glove in 12 tetraparetic subjects for performing activities of daily living8,9 and 2) evaluation of the effects of use of the Belgrade Gasping System (BGS) in 8 tetraparetic subjects10. In both studies chronic patients were assisted for prolonged time with multi-channel electrical stimulation system. In these two studies the subjects were used as self-controls since they were in the chronic stage of disease. In both studies subjects were given the device to use it as much as possible for performing daily tasks such as eating, drinking, moving objects, etc. The device was used unilaterally and applied over the dominant arm. The outcome measures in both studies included, among others, the functional independence measure (FIM) and the quadriplegia index function (QIF). The period of use of the assistive system was six months and included daily use in the clinical environment and at home.

The finding that we are emphasizing (Fig. 1) is that the FIM and QIF significantly increased in all study subjects without the as-

Table 1: The upper extremity function test and the drawing test results for the higher functioning group (HFG) and the lower functioning group (FFG). The asterisk denotes statistical significance between the subjects in the FET and control groups.

	Week 0 (before therapy)	Week 3 (end of therapy)`	2 months (follow up)	6 months (follow up)
Higher Functioning Group (HFG)				
Upper Extremity Function Test				
FET group	5 ± 3	18 ± 7*	27 ± 8*	26 ± 9*
Control group	6 ± 4	10 ± 6	12 ± 8	15 ± 7
Drawing test				
FET group	40 ± 5	62 ± 9*	74 ± 10*	82 ± 5*
Control group	40 ± 3	52 ± 9	60 ± 16	61 ± 12
Lower Functioning Group (LFG)				
Upper Extremity Function Test				
FET group	0	2 ± 1	4 ± 2	5 ± 2
Control group	0	1 ± 1	1 ± 1	2 ± 1
Drawing test				
FET group	15 ± 8	28 ± 9	36 ± 10	43 ± 8
Control group	15 ± 4	18 ± 4	24 ± 8	30 ± 12

sistive system after six months. This result suggests that, although subjects were in the chronic phase of tetraplegia (i.e., more than one year after spinal cord injury), voluntary movements in subjects were regained due to intensive exercise and possibly due to the application of electrical stimulation to augment function.

The second example comes from more recent studies in subjects with hemiparesis.[11,12] The electrical stimulation was delivered by UNAFET 4 (Una Sistemi, Belgrade, Serbia) and Actigrip® (Neurodan A/S, Aalborg, Denmark). Both devices apply four channels of electrical stimulation *via* self-adhesive surface electrodes positioned over the dorsal and volar aspects of the forearm. The stimulation pattern mimicked the sequence of prime movers of the fingers and the thumb typical for grasping in healthy individuals. The outcome measures in these studies included the upper extremity functioning test (UEFT) and the drawing test (DT), both specifically selected to assess the regained reaching and grasping abilities (without stimulation). The UEFT[13] test is the measure that shows how many times individuals can grasp, use and release the test object during two-minute intervals; thus, it is an integral measure of function (reach the object, open the hand and grasp, open the hand and release the object, and return to the initial position). Eleven test objects were included to assess the abilities for palmar, lateral and precision grasps. The DT[14] assesses the ability of subjects to manipulate, that is, to coordinate the shoulder and elbow joint, and does not consider at all the grasp. Patients were required to draw a square (20 cm x 20 cm) by moving the magnetic mouse over the digitizing board, and the measure was the ratio between the surface area surrounded by the drawn "square" and the surface of the target (400 cm^2), expressed in percent.

In this study, we stratified the analysis by dividing subjects into two groups: a higher functioning group (HFG), which consisted of subjects who entered into the study with the ability to voluntarily extend the wrist and fingers more than 10 degrees against gravity; and a lower function group (LFG), which consisted of subjects with basically no voluntary wrist and finger extension. The outcomes for the HFG and LFG were very different, as it can be seen in Table 1 generated from the results presented in Popović et al.[11]

The results show that there was a significant improvement and carry-over effect in the HFG; however, there was only a marginal improvement in the LFG. This is likely because the applied electrical stimulation was not sufficient to provide function because the level of disability was too high and prevented their reaching movements. The subjects from the LFG also required the assistance of proximal joints to be able to manipulate their hands, not only for grasping assistance. Electrical stimulation of proximal joints is much more complex, and there is no effective system that is applicable yet.

Robotics for therapy of subjects with ULD

As presented earlier, the use of electrical stimulation is suitable for control of the hand and possibly for hand orientation. The control for arm manipulation should be however assisted with haptic robots. The application of robots as aids in the treatment of persons with motor disabilities is reviewed in Prange et al.[15] and Kwakkel et al.,[16] and the indications are that robot therapy may be effective in accelerating the recovery of stroke patients. The main goal of rehabilitation robots is to "teach" subjects the correct movement trajectories of the proximal joints by manually moving their upper limb. This can be considered as "training for the brain."

Robotic guidance has been shown to improve motor recovery of the arm following acute and chronic stroke in two different ways:[17-20] 1) as "artificial therapists," and 2) as feedback in learning the movement. As artificial therapists, robots may be programmed to implement a variety of highly reproducible and repetitive training protocols. As feedback systems, robots detect all aspects of movement and can provide haptic interaction with the subject.

These two features are of importance since they allow the following: 1) exercises tailored to the specific impairment patterns of each subject, and 2) adaptation to the improved performance. The amount of force a subject is contributing to a movement varies widely in relation to impairment levels. The motor system tends to behave as an optimizer, which exploits the assistive forces generated by the robot in such a way that it reduces the degree of voluntary control (and therefore muscle activation). As a consequence, an assistive strategy that maintains a constant level of assistive force throughout the sessions would progressively depress voluntary control instead of promoting it.

Direct stimulation of the central nervous system

When considering how to further improve therapy, one should consider direct cortical stimulation. Namely, neuroscience research has provided strong evidence that stimulation of the brain leads to changes in cortical excitability. Brain stimulation can up- or down-regulate the excitability of lesioned and intact hemispheres, which could be used to facilitate re-learning and might ultimately lead to recovery of function in stroke patients. The possible mechanisms mediating these effects may include the correction of an abnormally persistent interhemispheric inhibitory drive from the intact hemisphere to the lesioned hemisphere in the process of the generation of voluntary movements by the paretic hand, a disorder that is correlated with the magnitude of impairment. The three techniques for brain stimulation are as follows: 1) transcranial magnetic stimulation (TMS), 2) direct transcranial current stimulation (dTCS), and 3) epidural cortical stimulation (ECS).[21-23]

Transcranial magnetic stimulation uses a rapidly changing magnetic field generated by a coil positioned closely proximal to the skull bone to painlessly induce controlled electrical currents in well-targeted regions in the brain. Repetitive TMS (rTMS) produces sustained changes in cortical excitability and regional brain activity. Low-frequency rTMS (0.2–1 Hz) consists of a single continuous train of pulses, whereas high-frequency rTMS (5–20 Hz) employs intermittent bursts. High-frequency rTMS can also be applied in continuous mode (> 100 pulses). Long-term synaptic changes explain why the effects of rTMS persist for a few hours after treatment. Repetition of sessions can reinforce and prolong rTMS after-effects. In addition, methods that can increase the duration and size of rTMS after-effects and produce substantial changes in cortical excitability have been introduced.[24-26]

Direct transcranial current stimulation is a technique that involves generating weak constant direct currents by placing electrodes directly on the scalp.[27] In general, cortical excitability is reduced by cathodal dTCS and increased by anodal dTCS, likely due to neuronal hyperpolarization/depolarization.[28] The direction of the polarizing effects, however, depends strictly on the orientation of dendrites and axons in the induced electrical field. In addition, both inhibitory and excitatory networks can be affected by DC stimulation.

Epidural cortical stimulation (ECS) depends highly on various technical parameters, including stimulation frequency and intensity, pulse width, duty cycle, montage (monopolar *vs.* bipolar), electrode polarity (anode *vs.* cathode) and the distance between the electrodes and neural elements.[29] The stimulator is implanted epidurally near the regions of interest to be activated. It has been suggested that the thickness of the cerebrospinal fluid layer between the dura mater and the underlying cortex affects the strength and the distribution of the electrical field induced in the brain.[30,31]

Conclusions

The cumulative results of the current research lead us to suggest that repetitive, active movement mediated by electrical stimulation and the use of robots within one system that can enhance motor re-learning following damage to the CNS is the optimal approach to rehabilitation. The term "motor re-learning" should be hypothesized to be a set of processes associated with practice or experience that lead to long-term changes in the capability of movement.

To meet the requirements for effective rehabilitation, the following objectives need to be addressed in future studies: 1) to improve the model of the human sensorimotor systems for effective application of electrical stimulation and assistive robots; 2) to develop methods for the integration of biological control, electrical stimulation and rehabilitation robots; 3) to improve the command interfaces for the integrated use of rehabilitation robots and electrical stimulation; and 4) to integrate brain-controlled rehabilitation technology and virtual reality-based feedback in rehabilitation.

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