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CEREBRAL PLASTICITY IN POST-STROKE REHABILITATION

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SUMMARY

Primary objective: *The plastic changes described in this study enable regeneration and compensation of damage to the nervous system. They can also explain the capacity for adaptation, modification, and organization, as well as the strength of neuronal connections when stimulated. The adaptive ability of the brain and its plasticity are more and more frequently used in post-stroke rehabilitation in order to reactivate all the regenerative capacities of the nervous system. In this review article the authors undertake an analysis of works on cerebral plasticity in the rehabilitation of patients after stroke.*

Main outcomes and results: *Methods based on cerebral neuroplasticity give significantly better results than traditional therapy. Recent studies confirm the beneficial effect of physical activity, such as early post-stroke rehabilitation, on the processes of compensation and cerebral activation, as indicated by plastic changes taking place in the brain.*

Conclusions: *Cerebral neuroplasticity based on intensification of natural plastic processes is an important aspect of post-stroke therapy. It gives a new perspective for scientific development in treating these patients. The challenge for contemporary medicine is to understand the mechanisms connected with cerebral plasticity and their modification in order to obtain the best behavioral results.*

Key words: *adaptation, regeneration, physical activity*

INTRODUCTION

For many years it was believed that brain tissue possesses little or no capacity for compensation and repair. At present it is thought that the basic pattern of connections between nervous system centers forms in development based on the genetic program; however, the neuronal circuits are plastic and modifiable throughout human life. Many neurons show only temporary functional disorder, and due to quick therapeutic actions they can be saved. This is possible due to a congenital feature of the human brain – the neuroplasticity of the nervous system, which can compensate defects given appropriate stimulation (Kułak & Sobaniec 2004; Pascual-Leone et al. 2005).

After excitability, cerebral plasticity is the second basic feature of nervous cells due to which there are permanent functional transformations originating from the definitive neural systems as a result of specific sensory stimulation or their combined activity. Appropriate stimulation of the neurotransmitters and growth factors gives better rehabilitation results (Carey et al. 2006; Kelly et al. 2006). It has been demonstrated that in the peripheral region of the necrotic focus there is a penumbra zone, a zone of relative ischemia dividing it from the tissue well supplied with blood, where many neurons manifest only functional disturbance. Blood reaches the tissue via the peripheral circulation. At the beginning, the changes may be reversible, but prolonged hypoperfusion or hypokinesis can lead to tissue necrobiosis also in this region. Rapid commencement of rehabilitation and restoration of correct circulation prevents the occurrence of irreversible changes, limiting the region of permanent ischemic damage that cannot be saved in the case of neurological patients. These are living cells able to take up their regular function, to save the inactive neurons, thereby also decreasing the necrotic region (Carey et al. 2006; Hakim 1998).

As mentioned above, spontaneous neuroplasticity is excited by neurorehabilitation. The key to the elaboration of the brain's post-stroke rehabilitation strategies results from comprehensive study of the phenomenon itself. The majority of motor tasks carried out by healthy persons give the performer an instant motor reply, and therefore outcome knowledge. Since patients with motor dysfunction frequently have sensory and perceptual problems, they are highly dependent on the therapist. This dependence is especially important in the early stages of therapy, when the task is completely new and the patient's main effort is directed towards comprehending what should be done and how to do it. Clear, simple instructions refer to repetition; motion which is accidental at first becomes more and more significant, and after some time approaches regular voluntary motion. Information coming to the brain leads to the creation of proper sensorimotor associations, and the motion is more and more precise. With the passage of time, the external stimuli supplied by the therapist are eliminated and the patient starts to perform the intentional action. This is so-called "motor teaching" (Classen et al. 1998; Sacco 2006).

After damage to the local cerebral cortex, therapy should lead to a "central fatigue"; then the central nervous system begins to work independently, the so-called autostimulation; not only can patient prognosis be improved, but also the quality of life (Sacco 2006; Pasek et al. 2007).

The plastic changes which are described in this study are the basis for regeneration and compensation of damage to the nervous system. They can also be explained as the ability to adapt, modify, organize and reinforce neuronal connections when stimulated. Contemporary neurobiology admits a broad definition of neuroplasticity. It comprises permanent changes in nerve cell properties occurring as a result of environmental stimuli or damage to the nervous system. At the systematic stage, plasticity is a feature of the nervous system which assures its capacity for adaptation, variability, self-repair, learning and memory. It is a common neural feature, found at all levels of the nervous system (Kossut 2005; Butefisch et al. 2000).

In contrast to plastic changes caused by peripheral nerve damage or by changes resulting from functional activation or deactivation occurring in a properly functioning healthy brain, the compensating plasticity of a damaged brain in patients after cerebral stroke acts in a completely different environment, interacting with inflammatory processes, edema, metabolic function disorders, necrosis, apoptosis and fibrous degeneration (Schaechter et al. 2008). Additionally, serious post-stroke biochemical and functional changes can be observed in the hemisphere opposite the damage. A characteristic sequence of advantageous post-stroke plastic changes connected with rehabilitation has also been described. Researchers in Warsaw have observed that the functions of damaged cerebral cortex regions are taken over by the cortex of the opposite hemisphere for up to several days. Then, several weeks after the stroke, the cortical representation of functions returns to the original hemisphere, but in a new, undamaged place (Cybulska-Kłosowicz & Kossuth 2006).

Observations of the cerebral reparatory mechanisms involved in plastic changes have shown that in a short period after the stroke, cerebral plasticity is not increased at all: quite the contrary, it is diminished. A post-stroke brain has trouble with almost everything: oxidation, neuronal nourishment, water and electrolyte balance. The neurons present in such a brain are exposed to a high level of stress. "Forcing" plastic changes to work increases their metabolic level and thus decreases tolerance for disadvantageous conditions (Kossut 2005; Jablonka et al 2007).

Experimental trials carried out on animals after stroke were first performed in the 1950s. Researchers damaged the cerebral cortex of rats in a place representing the hind paw; several months later the cerebral cortex was mapped. The study revealed that the removed representation of the paw muscle had been reconstructed in a place adjacent to the damage (Napieralski et al. 1998).

Another trial assessed qualitatively the relation occurring between cortical-spinal damage and the functional improvement and reorganization of the

cerebral cortex in patients after cerebral stroke. Application of MRI and CT showed that functional improvement connected with cerebral plasticity is related to the level and type of cerebral damage (Schaechter et al. 2008). These conclusions have been confirmed by the results of other studies (Sung et al. 2005).

MRI mapping of cerebral activity in patients after a stroke to the sensory and motor regions of the cortex frequently reveals excitations connected with movement performed by the hemisphere opposite the damage, and also by the region surrounding the lesion (Binkofski & Seitz 2004).

A 2005 study of patients with a stroke to the motor cortex revealed that the return of normal finger movement is connected with the shift of activation in the motor cortex in the region more dorsal in comparison to a control group of healthy persons (Jaillard et al. 2005).

Equally interesting are the results of other studies showing the connection between plastic changes and gaining new abilities after four weeks of rehabilitation. Motor exercises engage a specific muscle group. The muscular involvement is higher when the activity is complicated, new, requiring great precision, which is reflected in cortical changes in the regions adjacent to the damaged areas (Butefisch et al. 2000).

The process of acquiring new skills connected with nervous system plasticity has also been studied by American authors. They endeavored to determine the size and effectiveness of cerebral cortex changes in two groups of patients performing simple and complex movements repeated over a short period of time. The studies revealed that even a small motor stimulation (5-10 minutes) caused changes in the motor representation of the brain (Classen et al 1998).

French et al. (2008) analyzed electronic databases (2006-2008) in order to assess the therapeutic effects, costs and results of functional rehabilitation of the upper limbs. The results of the analysis proved that functional improvement is possible at every stage of rehabilitation, but the persistence of the results of individual therapeutic interventions was unclear. The performance of more complex activities required greater financial expenditure.

Another mechanism using the occurrence of excitations quickly following one another and coming from different sources is the integration of stimuli coming from apical and basal dendrites in short intervals of time on the pyramid neuron's dendritic tree. Very often this mechanism is used in neurorehabilitation, activating the brain with the help of stimuli of different modalities, thus leading to reactivation of all the regenerative abilities in the nervous system (Kossut 2005).

Modern methods based on cerebral plasticity are being introduced in specialist neurological rehabilitation centers. Beside PNF *(Proprioceptive Neuromuscular Facilitation)* and NDT Bobath *(Neuro Developmental Treatment)*, more and more frequently CIMT (*Constraint – Induced Movement Therapy*) is used in the rehabilitation of a paretic upper limb (Suputtitada et al 2004;

Taub et al 2003). In the 1990s Edward Taub from Birmingham University devised a forced movement therapy, wher, considering the general assumptions, the method is based on the immobilization of the non-paretic upper limb with the help of a sling in order to force intensive training of the paretic limb with its simultaneous intensive rehabilitation. The effectiveness of this rehabilitation method manifests itself mainly in greater activation of the paretic limb, which in turn is reflected in the performance of daily activities (Page & Levine 2007; Taub et al. 2002; Blanton et al. 2008).

In one of the US trials, the authors compared the effectiveness of the CIMT program to therapy carried out without CIMT in patients who had suffered a stroke within the previous 12 months. During the whole therapy period, the patients also received pharmacotherapy. After carrying out the rehabilitation cycles, the patients with the CIMT method showed a significantly higher statistical and clinical improvement in the range of upper limb functions of strength, grasp and motor coordination, studied with the help of scales assessing the functions of the upper limb, as compared to the control group (Wolf et al. 2005). The analysis of these studies suggest that, despite the passage of time, these patients still possess a potential for motor and functional improvement (Duncan et al. 2005; Perry & McLaren 2004).

Hummel and Cohen presented in their study the issue of the neuronal mechanism connected with cerebral plasticity and its capability in adaptation to the changes occurring under the influence of a past stroke in adults. This feature of the nervous system enables the learning of compensation for functional deficits, thus creating promising neurorehabilitation possibilities (Hummel & Cohen 2005).

A great deal of attention has also been drawn to unilateral neglect in the field of contemporary neurological rehabilitation. It is one of the more insidious neuropsychological problems, due to its variable clinical picture, the asymmetry of determining factors, the complexity of spontaneous recovery, and still open questions concerning the rehabilitation methods for patients with this disorder. This dysfunction can be described as a deficit in the active searching for and responding to stimuli coming from one side of one's own body parts and from the extrapersonal sphere located on the side opposite to the cerebral damage, which cannot be explained by basic sensomotoric deficits. Although neglect usually decreases with time, patients with this disorder need professional neuropsychological and physiotherapeutic treatment. Neglect, unlike most other focal cognitive deficits, has a negative impact on the majority of spheres of human activity. It has been revealed that patients with hemiparesis and neglect are less motor efficient in everyday situations than patients with similarly intense paresis but with no features of neglect; thus they require longer physiotherapy in order to obtain comparable therapeutic effects. In the most severe cases neglect disorganizes the performance of even the simplest activities; in less serious cases, it causes behavioral disturbances. Even a mild neglect may cause disturbed function-

ing as the complexity of the stimulatory situation increases. Numerous studies claim that various therapy forms lead to diminishment of the neglect symptoms and prevent its secondary results, but this requires further research. The majority of techniques refer to sensory-perception aspects of neglect, especially in the occular modality (Polanowska & Seniów 2005), but there are also interventions aiming at improving behaviors in other cognitive and motor spheres which can be disturbed in neglect syndrome, e.g. attention (Pachalska et al. 2005).

Another objective study discussed the issue of cerebral cortex plasticity with reference to interhemispherical reactions, combined with transfer of information and learned associations, directed attention, bilateral motion coordination, and coherent body surface perception. The results of studies carried out in this area have been consistent. Stroke-induced cerebral damage disturbs balance and frequently causes increased activation of the cortical regions of the other hemisphere, which may be conductive to the creation of compensating plastic changes in these regions. However, there are animal trials that suggest otherwise, and reveal that plasticity in the hemisphere opposite to the lesion is diminished. This problem, obviously important in neurorehabilitation, requires further research (Cybulska-Kłosowicz & Kossuth 2006).

Recent studies confirm the beneficial effect of physical activity, including early post-stroke rehabilitation, on the processes of compensation and cerebral activation, as documented by plastic changes taking place in the cerebrum (Tokarski et al. 2007). It is now believed that patients with moderate cerebral damage obtain significantly better results than those with severe damage (Adams et al. 2007). The best results are gained within three to six months of rehabilitation. Generally in this period the recovery of functions takes less time (starting from onset) and the therapeutic effect is the most beneficial.

Based on the literature it can be concluded that neurorehabilitation based on cerebral plasticity should be introduced with a slight delay, a few days after the stroke. Traditional methods, such as motor exercises (kinesitherapy), take place significantly earlier: immediately after the clinical stabilization of the patient, the second day after the stroke (Jablonka et al. 2008; Diserens et al. 2006). Confirmation of these observations requires further clinical research.

SUMMARY

The application of methods based on cerebral neuroplasticity gives significantly better results than traditional therapy. Cerebral neuroplasticity based on intensification of natural plastic processes seems to be a valid approach to post-stroke therapy. It gives a new perspective for scientific development of ways to treat the symptoms. The challenge for contemporary medicine is to understand the mechanisms connected with cerebral plasticity and their modification in order to obtain the best behavioral results. Progress in neu-

rorehabilitation has been and will be irreversibly connected with cerebral plasticity, which is already bringing beneficial therapeutic and rehabilitation results.

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