Rehabilitation after a stroke is undergoing a renaissance of sorts, with growing evidence of rehabilitation’s impact extending from cortical reorganization to its effect on health-related quality of life.

Functional Neuroimaging

Functional recovery after focal brain lesions is dependent on the adaptive plasticity of the cerebral cortex and of the nonaffected elements of the functional network. For the motor system, it has been convincingly demonstrated that after cortical injury the adjacent spared cortical tissue as well as more remote cortical areas are altered resulting in a functionally modified network. Small lesions in the somatosensory cortex lead to changes of excitability attributable to down-regulation of GABAA-receptors and up-regulation of NMDA-receptors in remote brain areas, and these changes in both excitatory and inhibitory neurotransmission may be part of an adaptive process involved in functional reorganization. As a consequence, newly learned movements after focal cortical injury are represented over larger cortical territories, an effect which is dependent on the intensity of rehabilitative training. Along with these changes in excitatory and inhibitory neurotransmitter systems, widespread structural changes with dendritic sprouting and synapse formation take place in spared regions of the damaged hemisphere, but also in the sensorimotor cortex of the hemisphere contralateral to the injury. One could speculate that the change in excitability in adjacent and contralateral homotopic regions of a cortical lesion is a consequence of reduced collateral and transcallosal inhibition.

It was also convincingly demonstrated that specialized areas inhibit neighboring regions and (even contralateral) brain regions connected by fiber pathways. Recent repetitive transcranial magnetic stimulation (rTMS) studies gave evidence that unilateral stroke lesions indeed reduce transcallosal inhibition and that the unaffected hemisphere actually inhibits the generation of a voluntary movement by the paretic hand. Increases in relative cerebral blood volume in contralateral brain regions connected by fiber pathways, indicate overactivation of right language homologues, which may represent a maladaptive strategy. This “paradoxical functional facilitation” can be interpreted as a result of decreased transcallosal inhibition attributable to damage of the specialized and lateralized speech areas. As a consequence, suppression of the (paradoxical) activation in these right hemispheric language homologue areas by slow rTMS improved naming in chronic, nonfluent aphasia patient.

Changes in the interaction within the functional network of language are important for the recovery from aphasia after stroke. In particular, studies of changes in the activation patterns during speech tasks have demonstrated that patients with favorable recovery predominantly activate structures in the ipsilateral hemisphere, but some activation was also seen in the right hemisphere. Despite such responses in the right superior temporal gyrus and in the inferior frontal gyrus, efficient restoration of language is usually achieved only if left temporal areas are preserved and can be re-integrated into the functional network. It was also suggested that the increased activation within the right hemisphere may be a marker of failed or faulty recovery attempts in the sense of maladaptive plasticity or the breakdown of normal interhemispheric control within the distributed neural network.

The role of activation in the right hemisphere for residual language performance can be investigated by combining rTMS with functional imaging (eg, positron emission tomography). Such an approach was used in 11 patients with aphasia 2 weeks after left sided middle cerebral artery infarction. rTMS stimulation sites were selected according to maximum flow activation within left and right inferior frontal gyrus (IFG). Of these patients 3 activated the left and 8 activated the bilateral IFG. rTMS resulted in increased reaction time latency or error rate in the semantic task in 5 patients with right IFG activation, indicating essential language function. In a verbal fluency task, these patients had a lower performance than patients with effects of rTMS only over the left IFG, suggesting a less effective compensatory potential of right sided network areas.

The concept of the different efficacy of intra- and interhemispheric compensation, attributable to collateral and transcallosal disinhibition, may be even taken 1 step further: stimulation of the motor cortex improves ipsilateral finger movements and performance in Purdue Pegboard test by functional facilitation of the unstimulated counterpart cortex because of suppression of transcallosal inhibition. This result suggests an interhemispheric rivalry and explains an abnormally high inhibitory drive from the motor area of the intact hemisphere to that of the lesioned side. The blockade of the contralateral intact area by rTMS, therefore,
can be used to modulate these inhibitory interactions, to influence motor disability, to improve attention to ipsilateral targets and to reduce hemispatial neglect.38–41 In a preliminary study in patients with nonfluent aphasia 5 to 11 years after left hemisphere-stroke, Naeser et al40 observed significant and persistent improvement in naming pictures after rTMS application to the pars triangularis of the right inferior frontal gyrus (homologue to Broca’s area). The authors postulated that rTMS decreased excitation in right BA 45, which in turn modulated activity in the distributed, bihemispheric language network. This result suggests the paradoxical effect of contralateral facilitation attributable to transcallosal disinhibition and supports the inferior capability of interhemispheric compensation for language recovery. The clinical and long-term efficacy of this novel complementary treatment for aphasia, however, must be proven in larger clinical trials.

**Clinical Rehabilitation Strategies**

Despite the excitement generated by early thrombolysis in acute stroke care, the greatest advancement in stroke care continues to be the stroke unit. Although stroke units are often thought to represent organized specialized stroke care, there is now overwhelming evidence of the effectiveness of interdisciplinary stroke rehabilitation units, but less clear evidence of effectiveness of organized stroke care during the acute phase. Gilligan et al.,42 based on the community-based NorthEast Melbourne Stroke Incidence Study, estimated that if different treatment strategies available for stroke patients were maximized, stroke units would reduce death and dependency of 46 of every 1000 stroke patients, a number over 4-fold greater than that of tissue plasminogen activator (assuming 10% of all stroke patients receive tissue plasminogen activator).

Although it is well recognized that stroke patients who receive organized in-patient stroke unit care are more likely to survive, be discharged to home, and achieve independence again, there remains uncertainty as to what elements of the “stroke units” are contributing to this improvement. The Stroke Units Trialists Collaboration43 in a systematic review of 29 clinical trials used a direct and indirect comparative analysis against conventional care on a general ward, using death and dependency as the critical outcomes. They found that acute-subacute combined stroke units, subacute rehabilitation units, and mixed rehabilitation units all resulted in significant reductions in death and dependency, while results were trending toward a benefit in the acute semi-intensive stroke units. Clinical outcomes appear to be better in stroke units because of greater adherence to processes of care.44,45 Moreover, it is becoming increasingly apparent that it is the interdisciplinary stroke rehabilitation therapeutic environment that appears to account for much of the success of “stroke units”. The success of stroke units appears to be more a consequence of stroke rehabilitation therapies than acute intensive medical monitoring although more research is needed.

Comprehensive stroke rehabilitation units are expensive, but mobile stroke teams do not confer the same benefit46 and have no major impact on death, dependency, or the need for institutional care when compared with care in general wards47 along these lines, Kalra et al48 compared the outcomes between stroke patients managed on a stroke unit, on general wards with stroke team support, or at home by a specialist homecare team. Stroke units were discovered to be more effective than a specialist stroke team or specialist homecare in reducing mortality, institutionalization, and dependence following stroke. Stroke unit care was a more cost-effective intervention than either stroke team or stroke homecare. Meta-analysis of research on early supported discharge shows benefits for coordinated multidisciplinary early supportive discharge teams in stroke patients with only mild to moderate disability.49

One concept which is becoming increasingly recognized is that not only is the brain capable of reorganization poststroke as we have stated earlier but that the brain is primed to recover early after a stroke and that delays in rehabilitation will reduce the opportunity for maximal neurological recovery.50 Hence, the statement “time is brain recovery” appears to hold true for rehabilitation. There is also a greater appreciation from the animal data of the benefits of keeping stroke patients active in a stimulating environment, which presents a real challenge where rehabilitation resources are limited. Moreover, Yagura et al51 were able to demonstrate that patients with severe strokes, where cortical reorganization is less of an issue, nevertheless appear to benefit the most with an interdisciplinary team approach in that a greater number of them are able to return home at the time of discharge, pointing out the importance of discharge planning to the success of stroke rehabilitation units for severe strokes. Finally, Paul et al52 found 20% of first-ever strokes assessed 5 years poststroke onset were found to be suffering from a very low health-related quality of life. Having established the efficacy of stroke rehabilitation in improving poststroke survival, functional outcomes, and improved discharge destination, future emphasis in stroke rehabilitation will be on improving health-related quality of life.

**References**
