Recent Advances in Stroke Rehabilitation 2006
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Stroke rehabilitation has benefited from significant advances in the understanding of the natural history of recovery after stroke and the developments of techniques to modulate recovery processes over the last year. The confluence of literature from basic preclinical sciences and human neuroimaging studies has resulted in new insights into the mechanisms of neuronal recovery and cortical reorganization after ischemic injury. There have also been a number of studies that seek to evaluate the efficacy of interventions based on better understanding of recovery processes. The last year has also seen an explosion of meta-analyses on the effectiveness of different therapy techniques in stroke rehabilitation, which have provided valuable information on the validity of various approaches to rehabilitation, previously restricted by sample size considerations.

Advances in the Mechanisms of Recovery
Stroke rehabilitation is based on the concepts of neuroplasticity and reorganization of cerebral activity, the validity of which has been strongly supported in many functional MRI studies over the last decade. These studies have also shown the diversity and complexity of reorganization patterns, suggesting that the process of reorganization is dynamic and dependent on the nature of injury, substrates involved and the duration since the initial insult. More recently, hyperacute imaging studies have shown that early rapid recovery of function corresponds with successful reperfusion of the ischemic penumbra, suggesting that successful thrombolysis, optimization of collateral flow and even angiogenesis may be the first step for successful rehabilitation. Recent studies in acute recovery have also shown that the integrity of the corticospinal tract system is critical for motor recovery within the first 4 weeks of stroke, irrespective of involvement of the somatosensory system, providing a physiological explanation for the clinical observation of slower recovery in older people and those with underlying white matter disease. These studies also provide added incentive to identify therapies effective in protecting axons as well as cell bodies. The concept shift away from strict localization of function to one anatomic site and toward multiple widely distributed pathways has been supported by previous studies showing that functional recovery correlates most closely with reorganization in ipsilateral peri-infarct and related contralateral cortical areas on functional MRI studies. Recent transcranial magnetic stimulation studies have shown that regression of perilesional inhibition and intracortical disinhibition of the motor cortex contralateral to the infarction play an important part in this reorganization. At the cellular level, ischemia appears to induce a unique microenvironment for surviving axons to sprout new connections and establish novel projection patterns in the first month after stroke. Poststroke neuronal regeneration may involve orchestrated waves of cellular and molecular events characterized by a reduction in growth-inhibitory molecules and activation of growth-promoting genes by neurons. In addition, there are waves of migration of immature neurons from their origin in the subventricular zone into peri-infarct cortex, partly mediated by the cytokine erythropoietin. These findings suggest that modulation of electrophysiological activity and/or manipulation of cellular and molecular events by novel therapies has the potential of improving recovery after stroke.

Another important emerging concept is that of “mirror neurons” which discharge during the execution of various hand-directed actions and during the observation of the same actions performed by other individuals. The mirror neuron system was first identified in the ventral premotor cortex and the inferior parietal lobule in monkeys, but a similar mirror neuron system has now been identified in humans. Furthermore, this system also has been shown to extend to mouth- and foot-directed actions. Recent studies have shown that this system performs an important role in action understanding, imitation learning of novel complex actions, and internal rehearsal of actions. These studies support the use of motor imagery as a novel approach for the treatment of stroke patients with motor impairments. Because interventions through the mirror neuron system may offer an alternate access to motor networks independent of the affected primary motor cortex, motor imagery–based interventions may prove particularly beneficial in patients in whom active movement therapies cannot be undertaken. However, literature in this area remains limited and although studies in healthy volunteers show activation of the nonprimary but not of the primary motor structures during motor imagery, cortical activation patterns in stroke patients are not known.

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Novel Interventions in Stroke Rehabilitation

The basis of all stroke rehabilitation is the assumption that patients will improve with spontaneous recovery, learning and practice. Recent studies show that reorganization in the brain can occur with both recovery and learning but improves significantly in both with practice. It is also clear that motor learning mechanisms are operative during spontaneous stroke recovery and interact with rehabilitative training. In addition, studies suggest that retention of motor learning is best accomplished with variable training schedules and, for optimal results, rehabilitation techniques need to be geared toward patients' specific motor deficits. Several promising new rehabilitation approaches have been developed on theories of motor learning and include impairment-oriented training, constraint-induced movement therapy, electromyogram-triggered neuromuscular stimulation, robotic interactive therapy and virtual reality.

Recent studies in animals have shown that direct epidural stimulation of the primary motor cortex surrounding a small infarct results in improvement in motor function. Studies in stroke patients using noninvasive transcranial magnetic stimulation and direct current stimulation have similarly shown improvements in motor function. Lefaucheur has reviewed the first clinical results on the use of repetitive transcranial magnetic stimulation (rTMS) in patients with poststroke motor deficit, visuospatial neglect, or aphasia. Functional recovery was obtained either when rTMS was applied at low frequency (around 1 Hz) over the unaffected hemisphere in order to restore inhibition or when rTMS is applied at high frequency (5 Hz or more) over the affected hemisphere in order to reactivate hypoactive regions. There was great variation regarding the number of rTMS sessions required for a sustained effect and the timing of rTMS application after stroke, but the conclusion was that acute or recent stroke might be a major indication of rTMS in the future.

There have been a few small clinical studies exploring the concept of motor imagery in stroke rehabilitation, of which 4 are randomized controlled trials, 1 case-controlled study and 5 case reports. All studies were small and differed in patient characteristics, intervention protocol, and outcome measures. Most tasks involved mentally rehearsing movements of the arm, but intervention periods varied from 2 to 6 weeks and frequencies ranged from multiple sessions per day to 3 times a week. There was some evidence that mental practice as an additional therapy intervention had positive effects on recovery of arm function and may have promise for improving leg function after stroke. However, further studies are needed in this area, despite the known problems with contextual reliability, subject concordance and evaluation of outcomes.

Meta-Analyses of Established Therapy Interventions

A major limitation in the translation of therapy research into clinical practice has been the validity and generalizability of the findings of intervention studies because of the small sample sizes, variability in subject selection and differences in interventions or outcome measures. The emphasis on evidence-based management has resulted in a broader secondary analysis of therapy studies to validate their translation into clinical practice.

Early mobilization is seen as one of the key components of acute stroke care responsible for good outcomes. However, mobilization protocols remain poorly defined and vary both with geography and the nature of the unit on which patients are being managed. A recent review which combined data from observational studies and meta-analyses over the last 55 years was not able to find any positive, unequivocal benefit associated with early mobilization, independent of other aspects of stroke care. The only conclusion possible was that early mobilization was not harmful for most stroke patients and may well be beneficial in some patients, but no controlled studies exist comparing early (eg, 1 to 3 days) versus late (eg, 1 to 2 weeks) mobilization. The review concluded that although data were insufficient to prove the beneficial effects of early mobilization after stroke, early neurological rehabilitation as part of routine stroke-unit care contributed to good long-term outcome.

Restoration of motor function has been a key element of stroke rehabilitation, and the last year has seen several pooled data analyses of studies on various aspects of improving motor performance. A prospective meta-analysis to determine the overall effectiveness of bilateral movement training in poststroke motor rehabilitation showed that bilateral movements alone or in combination with auxiliary sensory feedback were effective in improving functional and mobility outcomes in stroke patients. The role of bilateral standing with visual feedback therapy to improve postural control for stroke patients, on the other hand, remains unproven because there were no significant benefits over conventional therapy for weight distribution and postural sway, balance and gait performance, and gait speed. There is evidence to support a role of peripheral neuromuscular electrostimulation in stroke rehabilitation because these techniques appear to improve aspects of functional motor ability, motor impairment and normality of movement compared with no treatment, placebo or conventional physical therapy. However, there was considerable heterogeneity between studies and insufficient robust data to recommend routine use of these techniques in mainstream clinical settings.

Research into service organization and strategies of provision of specialist rehabilitation to stroke patients has been responsible for dramatic improvements in stroke outcome in recent years. Larsen et al compared the benefits of early supported discharge managed by a multidisciplinary team that plans, coordinates, and delivers care at home with rehabilitation on stroke units. Management by the early home discharge team resulted in a significant reduction in institutionalization and length of hospital stay but mortality was unchanged. However, implementation in clinical practice was fraught with problems—not unsurprising in view of the complex nature of stroke care—requiring input from professionals, patients and carers. Few complex interventions in stroke care have been adequately developed or evaluated, which may explain failures to implement trial findings into clinical practice.
Disclosures

None.

References
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