Stroke Rehabilitation: Strategies to Enhance Motor Recovery

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Abstract

Recent evidence indicates that the brain can remodel after stroke, primarily through synaptogenesis. Task-specific and repetitive exercise appear to be key factors in promoting synaptogenesis and are central elements in rehabilitation of motor weakness following stroke. Expert medical management ensures a patient is well enough to participate in rehabilitation with minimal distractions due to pain or depression. Constraint-induced motor therapy and body-weight-supported ambulation are forms of exercise that “force use” of an impaired upper extremity. Technologies now in common use include robotics, functional electrical stimulation, and, to a lesser degree, transcranial magnetic stimulation and virtual reality. The data on pharmacological interventions are mixed but encouraging; it is hoped such treatments will directly stimulate brain tissue to recovery. Mitigation of factors preventing movement, such as spasticity, might also play a role. Research evaluating these motor recovery strategies finds them generally good at the movement level but somewhat less robust when looking at functional performance. It remains unclear whether inconsistent evidence for functional improvement is a matter of poor treatment efficacy or insensitive outcome measures.
Motor recovery: improvement in the strength, speed, or accuracy of arm and leg movements (“getting better”)

Functional recovery: improvement in performance, e.g., self care or walking (“doing better”)

**Introduction**

Stroke is defined as a sudden, focal neurological deficit due to a cerebrovascular abnormality and is the third leading cause of death in the United States, behind heart disease and cancer. There are about 600,000 new and 180,000 recurrent strokes each year in the United States; 1.1 million adults reported some degree of functional limitation due to stroke in 1999 (1). About 50%–70% of persons with stroke eventually regain independence, but 15%–30% are left with a permanent disability. At six months poststroke, 30% of survivors require assistance for walking and one quarter need help to perform activities of daily living (ADL) (1). Given the risk of age for stroke and the rapidly aging population of the United States, successful rehabilitation will have enormous public health implications over the next few decades.

The specific deficits seen after stroke depend on the area of the brain affected. Aphasia, dysarthria, dysphagia, neglect, pain, cognitive deficits, sensory loss, and depression are common and can be extremely limiting. Motor weakness may be the deficit most obvious to both patient and outside observer and is the primary focus of this review. Hemiparesis, the simultaneous weakness of an arm and leg on one side, is the most common pattern of weakness, seen in ~60% of cases (1). The severity of motor weakness is a strong predictor of the severity of functional deficits (2).

Rehabilitation medicine is the medical specialty that addresses and manages function, best thought of as “performance.” Neurology and neurosurgery diagnose and treat acute stroke, but rehabilitation professionals manage the residual deficits in communication, self care, and ambulation performance, i.e., function. Stroke rehabilitation is managed by health care teams that include physiatrists, sometimes neurologists, nurses, physical and occupational therapists, speech-language pathologists, social workers, and others. The rehabilitation team uses a variety of techniques to improve performance following stroke, such as strengthening of both weak and intact extremities, use of assistive devices and bracing, environmental modification at home and work, and prevention of further disability (3).

It is essential to distinguish motor recovery from functional recovery following stroke. Motor recovery refers to improvements in the strength, speed, or accuracy of arm and leg movements. These improvements occur as a result of both natural recovery and rehabilitation interventions. Functional recovery refers to improvement in performance, such as self care or walking. Although complex, functional recovery is determined by the type, severity, and resolution of motor deficits, the ability of the patient to learn and implement new strategies including compensation with the intact extremities, and the characteristics of rehabilitation therapy provided (its type, timing, quantity, frequency, etc.) (2). One can think of motor recovery as “getting better” and functional recovery as “doing better.” There is considerable debate over how much rehabilitation should emphasize compensation versus recovery (2, 4, 5).

**Mechanisms of Motor Recovery Following Stroke**

Motor recovery is also a multifaceted process. In the hours to weeks following a stroke, natural recovery depends on decreasing local edema, reperfusion of the ischemic penumbra, and resolution of diaschisis or areas of metabolically depressed brain distant from the infarction (2, 4). Natural recovery is passive, requiring neither effort nor learning by the patient. [Intravenous and intraarterial thrombolysis aimed at reducing infarction and restoring the viability of the ischemic penumbra also contribute substantially to recovery and have been recently reviewed in this journal (6).] Motor recovery can also be due to actual reorganization of brain tissue in and around areas of damage. This is an active process and requires considerably more time. The underlying mechanisms for late brain reorganization are likely related to increases in the absolute numbers and concentration of synapses on dendrites (7) and unmasking of
latent neural networks (5, 7). Sparing of the secondary motor cortex may be particularly important in longer-term motor recovery (2). This “rewiring” allows the motor cortex to shift the relative control of a given body part. It also appears to occur only as a result of the patient’s experience. Defining the optimal nature, characteristics, intensity, and timing of this experience constitutes the fundamental challenge in stroke rehabilitation.

The Patient’s Experience of Rehabilitation Following Stroke

In recent years, two factors have emerged as important for cortical reorganization and plasticity: task-specific activity and repetition (4, 8). For example, to improve walking, a patient must exercise the muscles used in walking and exercise them multiple times. In addition, several authors have pointed out the importance of integrating motor learning principles into the rehabilitation experience (9, 10). Other factors that may be critical to motor recovery include the emotional impact of the activity (is it important and enjoyable?), the concomitant use of tactile and visual stimuli, varying the task within and between exercise sessions, and the role of sleep in consolidating new motor skills.

Specificity and repetition of exercise underlie many rehabilitation interventions following stroke, including several of the technological and novel treatment approaches discussed here. The most effective strategy to maximize long-term motor recovery is likely a combination of acute interventions to salvage viable brain tissue and effective rehabilitation to remodel what viable tissue remains (4). This brief review highlights some established and emerging rehabilitation strategies to enhance motor recovery following stroke. The discussion is grouped into four categories: (a) medical and psychological management to maximize participation, (b) novel approaches to exercise, (c) technology, and (d) pharmacological strategies. We conclude with promising trends that may shape the future of stroke rehabilitation.

MEDICAL AND PSYCHOLOGICAL MANAGEMENT TO MAXIMIZE PARTICIPATION

If remodeling motor cortex following stroke requires active, specific, and repetitive exercise, then a patient must be able to participate. The management of medical complications, pain, and depression may help explain why care in organized stroke units reduces mortality and complications and improves recovery (4, 11). Langhorne & Duncan (12) recently estimated that “for every 100 patients receiving organized, inpatient multidisciplinary rehabilitation, an extra 5 will be returned home in an independent state.” A recent Cochrane review of 31 trials and 6936 patients concluded that persons with stroke who received inpatient care in a stroke unit were more likely to be independent and living at home one year poststroke (13).

Medical Issues

In a study of 663 patients with acute ischemic strokes, the most frequent infections were pneumonia in 10% and urinary tract infection in 13% of patients (14). Risk factors for developing pneumonia include atrial fibrillation, greater age, and congestive heart failure, all of which were independently associated with higher inpatient mortality and decreased ambulatory status on discharge. Swallowing is compromised in at least 40% of stroke patients, increasing the risks for pneumonia and dehydration. Most dysphagia is transient, with <2% of stroke survivors still dysphagic one month poststroke. Although limited by small samples and use of historical controls, a recent review concluded that poststroke dysphagia programs are accompanied by a reduction in pneumonia rates (15). Initial management of severe dysphagia includes diagnostic testing, such as modified barium swallow testing and fiberoptic visualization; nasogastric and percutaneous gastrostomy feedings; modified-texture oral diets; and swallowing exercises and maneuvers such as the “chin tuck.”
In the Post-Stroke Rehabilitation Outcomes Project (PSROP) database, 5.6% of 1161 rehabilitation patients developed a deep vein thrombosis (DVT) (16). Early mobilization, use of blood-thinning agents, and hydration may help prevent DVT. Use of heparin reduces the incidence of DVT and pulmonary embolism, and one indirect comparison of unfractionated and low-molecular-weight heparin (LMWH) suggests that low-dose LMWH is more effective in decreasing DVT and pulmonary embolism without a clear increase in hemorrhage (17). Although mechanical compression devices are widely used, there is limited evidence for their effectiveness in stroke.

Seizures occur in just over 3% of strokes at onset and are associated with a higher mortality at 30 days. A higher incidence is seen among hemorrhagic strokes and younger patients (18). Ongoing antiepileptic treatment is required in only 3% of cases within 7 years of the event (19). Age, intracerebral hemorrhage, lesion size, increasing stroke severity, and early seizures are independent predictors of poststroke epilepsy (i.e., recurrent seizures). Seizure prophylaxis is not routinely initiated following stroke, with the possible exception of large hemorrhagic strokes. Cognitive impairment and sedation associated with antiepileptic agents are a significant concern for rehabilitation participation.

Pain Management

A number of pain syndromes are seen after stroke, and effective management can greatly facilitate participation. Central poststroke pain (CPSP), formerly known as thalamic pain syndrome of Déjerine and Roussy, is a central neuropathic pain occurring in patients with subcortical strokes. The incidence of CPSP is at least 8% during the first year following stroke, with >60% experiencing onset of the pain within one month (20). Treatment is notoriously difficult and includes amitriptyline and lamotrigine as first-line and mexiletine, fluvoxamine, and gabapentin as second-line treatments.

Complex regional pain syndrome (CRPS) of the hemiparetic arm after stroke is also known as shoulder-hand syndrome. The etiology of CRPS is not entirely clear but may involve exaggerated inflammatory and abnormal sympathetic responses (21). Pain at the shoulder or hand, or both, occurs 2–4 months from stroke onset and is usually described as burning, continuous, and exacerbated by movement. Physical examination is remarkable for hand edema, changes in skin blood flow, allodynia, and hyperalgesia, and the elbow is typically spared. Other than physical interventions to reduce hand edema, oral steroids are probably the treatment of choice (21), followed by nonsteroidal anti-inflammatory drugs and anticonvulsants such as gabapentin. Nonpharmacological treatments include psychotherapy and transcutaneous electrical nerve stimulation.

The flaccid hemiplegic shoulder is particularly susceptible to glenohumeral subluxation. The relationship between subluxation and shoulder pain is not clear, however. Expert consensus recommends the use of lapboards or pillows to support the weak arm and minimize subluxation (22). The use of slings to reduce subluxation is controversial; slings should probably be used only during ambulation. Shoulder tape, electrical stimulation, intraarticular steroids, and botulinum toxin have all been described as effective treatments (22, 23).

Poststroke Depression

Depression is seen in up to 50% of persons during the 12 months following stroke (24). Poststroke depression is likely underrecognized and undertreated, partly owing to its subtle presentation, “minor depression with dysthymia” in 80% of cases. Several studies have identified a clear association between depression and both mortality and poor rehabilitation outcomes (24). Depression often thwarts rehabilitation participation through poor motivation or secondary attention and memory deficits that limit the learning of new skills. The prophylactic use of antidepressant medications has been recently reviewed and may hold promise (25). Once recognized, poststroke depression can be effectively and safely treated with either
selective serotonin reuptake inhibitors or tricyclic antidepressants (23).

**APPROACHES TO EXERCISE**

There are several philosophies of exercise to promote motor recovery following stroke. Until recently, there was little evidence favoring any one approach over another (8). The science behind exercise in neurological disease is not outstanding but does support a “weak, but significant dosage effect with conventional therapy” (26). Persons with stroke tend to avoid using an impaired extremity. This “learned nonuse,” originally described by Taub and colleagues (27, 28), may result from decreased cortical representation due to the stroke itself or “low spontaneous use” of the limb due to frustration or overemphasis of compensation using the intact extremities (28). Physical and occupational therapists look for opportunities to “force use” of a weak extremity to break this pattern and facilitate cortical activation (2).

**Constraint-Induced Movement Therapy (CIMT)**

CIMT magnifies the concept of forced use by requiring a patient to perform functionally oriented activities using only the paretic arm while the unimpaired arm is physically restrained with a sling or mitt. In addition, therapists provide hand-over-hand skilled guidance (“shaping”) to assist the weaker arm in repetitive functional tasks (28).

The Extremity Constraint Induced Therapy Evaluation (EXCITE) Trial was a multicenter single-blind randomized controlled trial (RCT) comparing CIMT to customary care in 222 persons within 3–9 months of a first stroke (29). Some degree of voluntary finger extension was required to qualify for the study. CIMT was provided over two weeks, during which shaping was provided by a therapist 6 h per day, 5 days per week, and a mitt was worn on the unaffected hand 90% of waking hours, including weekends. At one year, the CIMT group performed better on a series of timed, semi-functional tasks and on a subjective measure of hand function. The two-year follow-up documented no decline from one year, and there were even trends toward continued improvement (30). Recent kinematic data have also confirmed improvements in quality of movement as a result of CIMT (31).

CIMT is personnel-intense and costly, and there currently are no mechanisms for reimbursement (28). Several groups are exploring modifications of CIMT (less intense over longer time periods) that might increase its practicality (28). CIMT requires a remarkable degree of patient motivation, since the inability to compensate with the intact arm can be terribly frustrating. In the EXCITE trial (28), gains in speed and subjective patient assessment of arm use were more robust than gains in objective observations of arm ability or motor strength. The control group received only “usual and customary care,” which is a central point of criticism of the study because the CIMT group received a greater “dose” of exercise. Despite the study’s methodological weaknesses, maintaining gains two years after two weeks of exercise is rather remarkable.

**Body-Weight-Supported Gait Training**

Body-weight–supported (BWS) gait training is a novel approach to the enhancement of walking after stroke by means of forced use, specificity, and repetition (32). While suspended in a parachute-like harness hanging from a frame (see Figure 1), a patient is able to simulate and practice complex gait cycles. Some authors feel that even in stroke, spinal cord mechanisms may play a role in improving walking patterns (33). The effect of body-weight support is somewhat analogous to the buoyancy of walking in a swimming pool. Hesse (34) has estimated that BWS training can increase the number of steps in a treatment session from 50 to >1000. The therapy allows the patient to practice more nearly normal gait patterns and to avoid developing “bad walking habits” (35). BWS training can occur over ground, on a traditional treadmill,
in walking independence and functional status among the BWS/Gait Trainer group than in the traditional-therapy group in a single-blind RCT with equal treatment times between groups. Results are encouraging, but a better understanding is needed concerning the use of a handrail, the magnitude of body support, the intensity and length of training, and the speed of the treadmill (35).

TECHNOLOGY

The use of new technological strategies to improve motor recovery after central neurological disease, including stroke, has exploded over the past two decades. This technological revolution is in its infancy, but already there are questions about effectiveness versus cost.

Robotics

Robotics have been used widely to assist exercise and quantify movements in stroke rehabilitation over the past 15 years (38–40). Both upper (UE) and lower extremity (LE) units are commercially available, but published research is mostly on the UE devices. These focus on either proximal (shoulder, elbow) or distal (wrist, finger) muscles (see Figure 2a,b). Potential advantages over conventional therapy include increased intensity, more repetitions, better patient engagement, enhanced motor learning via additional visual stimuli, outstanding standardization of movements within and between sessions, and the ability to track patient response longitudinally over time (38–40). The most sophisticated units are haptic, i.e., they interface with the user via the sense of touch, and possess the ability to quantify patient performance and adjust future treatment parameters (38). There is evidence that distorting a patient’s movement, such as pushing the arm off course during a reaching activity, may actually increase effectiveness (38). One very small study (41) demonstrated that bimanual therapy may be less effective than unimanual, but this requires confirmation.

The efficacy of UE robotics for motor recovery is reasonably well established (38–40).
Stroke rehabilitation robotics. (a) The MIT-MANUS wrist unit focuses on flexion/extension and supination/pronation of the weak wrist after stroke. (b) The MIT-MANUS proximal arm unit provides or assists movement to the shoulder and elbow while the subject moves the cursor on the computer screen. (c) The Lokomat combines partial body-weight-supported treadmill training with active robotic control at the hip and knee and passive control at the ankle.

The most extensive work has used the MIT-MANUS and the MIME units. A recent meta-analysis of 218 patients (39) concluded UE robotic treatment results in improved UE motor recovery compared to traditional rehabilitation therapy, but no differences were found for performance-based measures. The best-studied LE device is the Lokomat (see Figure 2c) (40). Like the Gait Trainer, the Lokomat uses body-weight support, but it is larger, more complex, and more expensive. Initially used in spinal cord injury, the Lokomat provides active control at the hip and knee and passive control at the ankle. A recent, small RCT of Lokomat versus
conventional therapy in persons with stroke reported improvement in gait patterns and anthropometric measures among the treatment group, but no improvement in gait-assistance category or speed (42). A second, smaller, nine-week crossover study found Lokomat training superior to conventional therapy for gait and distance achieved on a six-minute walk (43).

**Functional Electrical Stimulation**

Functional electrical stimulation (FES) provides short, coordinated bursts of electricity to weak muscles to facilitate functional movement (44). FES can also be used to strengthen muscle, improve range of motion, and reduce spasticity. FES is not useful in the presence of lower motor neuron disease (i.e., peripheral neuropathy, radiculopathy) and probably has greater functional utility for the lower extremities.

There are two surface, peroneal nerve stimulators available in the United States and a third in Great Britain. LE FES stimulates the common peroneal nerve during the swing phase of gait, producing ankle dorsiflexion and eversion (see **Figure 3a**). This offsets the ankle equinovarus typically seen after stroke and results in easier clearance of the leg. A recent Cochrane review (44) concluded LE FES was beneficial compared to no treatment for gait and motor recovery, although the quality of research was generally poor. Not included in that review is a recent nonrandomized unblinded study reporting a 34% increase in walking speed and improved gait symmetry in 24 patients with stroke after 8 weeks of LE FES treatment (45). Another recent small study found a trend toward increased walking speed and improved performance on a functional mobility test with LE FES compared to a conventional plastic ankle-foot orthosis (46).

Several UE FES units are available, and despite mixed quality, the research in stroke supports a positive impact on motor recovery at the hand (see **Figure 3b,c**). Several studies report better outcomes among subjects having at least some degree of active movement of the

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**Figure 3**

Functional electrical stimulation. (a) Components of the Bioness L300 unit include the heel switch (not shown), the wireless transmitter on the inside of the shoe, and the proximal leg cuff providing stimulation to the peroneal nerve during the swing phase of gait. Other panels show the Bioness H200 stimulating full finger flexion (b) and extension (c), which can be used to simulate a functional grasp.
hand and fingers. In one of the better published studies, Powell et al. (47) randomized 60 subjects (mean time poststroke = 22 days) to 30 min FES for 8 weeks versus standard rehabilitation treatment. At 32 weeks, better motor recovery was reported in the FES group. The commercial availability of FES will undoubtedly increase its use, but further research is required to substantiate functional gains given the cost of the technology.

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) is a newer technological addition to stroke rehabilitation. TMS uses a magnetic pulse to noninvasively and reversibly disrupt electrical transmissions in the brain. It has been suggested that TMS produces “virtual lesions” of the brain. Thus, it can be used to map cortical changes in motor control resulting from an intervention such as CIMT (48). Repetitive TMS (rTMS) is used to achieve a longer-lasting effect, up to 15 min depending on the frequency of the pulse. At higher frequencies (10 Hz), TMS increases cortical excitability for a few minutes. TMS appears to be safe and very well-tolerated by subjects with stroke. In addition to brain mapping, Takeuchi and colleagues (49) recently reported improvements in motor movement when using TMS to stimulate the opposite hemispheric primary motor cortex—suggesting an inhibitory role for the contralateral motor areas. No side effects were noted.

Virtual Reality

Virtual reality (VR) uses computer technology to provide real-time input to multiple systems—sight, sound, and touch. These interactions are designed to be novel, fun, and specific to an individual’s needs, in accord with motor learning theory (9, 50). Some VR allows a patient to don a computerized glove that provides sensorimotor biofeedback to the paretic hand (i.e., CyberGlove and Rutgers Master II-ND). Other systems use goggles or special glasses to “immerse” the user in a virtual environment. Simpler, nonimmersive systems use a computer screen to simulate an experience, but the degree of immersion appears to be a factor in treatment success (50). The enjoyment of training encourages repetition, which promotes motor recovery. Systems are also available to facilitate walking activities (51). A recent review concluded that although effectiveness data are limited, VR training may lead to improvements in motor strength and walking. As with many of the technologies discussed, further and better-designed research is needed to evaluate VR.

Pharmacological Interventions

The idea of combining catecholaminergic medications and rehabilitation to improve motor function after acquired brain injury has been popular since Feeney’s classic animal studies in the early 1980s (52). The two medications most studied in stroke are d-amphetamine and levodopa. Animal studies have demonstrated that amphetamines increase noradrenergic and activity-dependent neurotransmission and neosynaptic growth in peri-infarction and contralateral brain tissue. Most authorities feel that medications should be temporally coupled with task-specific rehabilitation (53).

Human studies are mixed. Some find that 10 mg of dextroamphetamine before physical therapy facilitates motor recovery (54, 55) whereas others find no effect (56, 57). A recent study was better-powered with 71 subjects and still failed to find an effect of 10 physical therapy sessions coupled with 10 mg amphetamine (versus 10 sessions with placebo) (58). Side effects have generally been quite mild. Overall, a 2007 Cochrane review concluded that the data “suggested benefits on motor function” from amphetamines after stroke (59). A double-blind RCT (60) showed that a single dose of levodopa in patients with chronic stroke enhanced motor learning compared with placebo. Another randomized study of 53 stroke patients showed that a single 100-mg dose of levodopa plus three weeks of physical therapy resulted in better motor recovery than placebo and the
same exercise protocol (61). Larger trials with more aggressive dose escalations are warranted, given the minimal side-effect profile and trends toward better motor recovery.

**SPASTICITY**

The identification and treatment of functionally significant spasticity in persons with stroke is an area of increasing interest among rehabilitation professionals. The definition of spasticity as “velocity-dependent tone” on passive ranging of a joint is a clinically and scientifically inadequate description but is widely used nonetheless. From the patient’s standpoint, spasticity is an involuntary “muscle stiffness” that may or may not be accompanied by muscle weakness. There are many endpoints for treatment of spasticity, including decreased pain, improved range of motion, and enhanced hygiene of the palm and perineum. Enhancing underlying motor movement limited by muscle tone is an appealing, although debated (5), outcome.

A variety of medications are available. Baclofen and tizanadine are commonly used for mild to moderate generalized spasticity but sedation is a relatively frequent limiting side effect (62). Opinions differ on the effectiveness of oral agents in reducing tone, and data regarding the impact on functional motor parameters are rather limited (62). Intrathecal baclofen (ITB) delivered through a surgically implanted pump is a more recent treatment for moderate to severe generalized spasticity. The therapeutic effect of ITB is more prominent in the legs than in the arms. It is unclear if ITB alters long-term motor recovery after stroke, but the therapy clearly reduces spasticity (63). Data are less clear on the impact of ITB on gait speed and other gait parameters (63), but quality of life was significantly enhanced in a recent open-label trial (64). Importantly, ITB does not seem to have a detrimental impact on strength in the unaffected leg (63).

When moderate to severe focal spasticity limits function, botulinum toxin (BT) can be injected into the affected muscle. BT is particularly helpful for the smaller muscles controlling the hand and foot. Like ITB, BT clearly reduces spasticity and improves subjective disability. Recent data suggest a significant improvement of quality of life with several injections over a year (65, 66).

Orthopedic and neurosurgical procedures are also used if more conservative measures fail to alter joint biomechanics and improve range of motion and motor control (67). For all spasticity treatments, functional outcome needs to be more closely examined.

**FUTURE TRENDS IN MOTOR RECOVERY FOLLOWING STROKE**

The revolutions of stem cell transplantation and human genetics may hold promise for motor recovery following stroke. Manipulation of growth factors, stem cells, migration of neuroblasts, and targeted cell differentiation in
the brain could play a significant role in enhancing neurogenesis after stroke and other neurological disorders (68). Genetic testing might differentiate which patients respond best to rehabilitation intervention (69, 70). Future advances in neuroimaging will undoubtedly provide new insights, including a better delineation of mechanisms of motor recovery and quantification of physiological changes serving as a “biomarker” for treatment effect (69, 70). Technology will play an ever-expanding role in stroke rehabilitation. Among the most exciting developments are brain-computer interfaces that allow a subject to think about moving a robotic or other device while connected invasively (71) or noninvasively (72, 73) to a computer network. In the next generation of FES, already in limited use, surface electrodes are abandoned in favor of tiny, self-contained intramuscular or perineural implants called BIONs (see Figure 4) (74). Wireless activation of a series of BIONs could simulate functional movement of a hand or foot without using an external device. With very few exceptions, the strategies discussed in this review have been implemented and studied in isolation. The ultimate question may be how to combine simultaneous and sequential interventions at specific times poststroke to achieve the best motor and functional recovery (9).

DISCLOSURE STATEMENT

The authors are not aware of any biases that might be perceived as affecting the objectivity of this review.

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