REVIEW ARTICLE

Stroke Rehabilitation and Motor Recovery

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ABSTRACT

OBJECTIVE: **Up to 50% of the nearly 800,000 patients who experience a new or recurrent stroke each year in the United States fail to achieve full independence afterward. More effective approaches to enhance motor recovery following stroke are needed. This article reviews the rehabilitative principles and strategies that can be used to maximize post-stroke recovery.**

LATEST DEVELOPMENTS: **Evidence dictates that mobilization should not begin prior to 24 hours following stroke, but detailed guidelines beyond this are lacking. Specific classes of potentially detrimental medications should be avoided in the early days poststroke. Patients with stroke who are unable to return home should be referred for evaluation to an inpatient rehabilitation facility. Research suggests that a substantial increase in both the dose and intensity of upper and lower extremity exercise is beneficial. A clinical trial supports vagus nerve stimulation as an adjunct to occupational therapy for motor recovery in the upper extremity. The data remain somewhat mixed as to whether robotics, transcranial magnetic stimulation, functional electrical stimulation, and transcranial direct current stimulation are better than dose-matched traditional exercise. No current drug therapy has been proven to augment exercise poststroke to enhance motor recovery.**

ESSENTIAL POINTS: **Neurologists will collaborate with rehabilitation professionals for several months following a patient's stroke. Many questions still remain about the ideal exercise regimen to maximize motor recovery in patients poststroke. The next several years will likely bring a host of new research studies exploring the latest strategies to enhance motor recovery using poststroke exercise.**

INTRODUCTION

In the first hours after a stroke, neurologists work with emergency medicine physicians, interventional radiologists, and neurosurgeons to minimize infarct size by converting ischemic penumbra to salvaged brain tissue.[1] That salvaged tissue then translates into the preservation of limb movement, mobility, communication, cognition, and eventually independence. While neurologic interventions often focus on how damaged brain tissue relates to symptoms, rehabilitation interventions often focus on how symptoms relate to performance or function. Among the numerous manifestations of stroke, motor recovery typically predominates rehabilitation discussions partly because

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Dr O'Dell discusses several clinical trials involving the use of investigational drugs, none of which are US Food and Drug Administration (FDA) approved for use in people with stroke.

of its importance in physical independence but also because it is so obvious and observable.[2,3] The distinction between motor recovery and functional recovery in stroke rehabilitation is critical.[4]

Motor recovery is the partial or complete improvement of an individual's motor symptoms such as weakness, coordination, fine control, or ataxia. The patient **gets** better. Motor recovery occurs either passively, as the hostile environment at the site of stroke resolves,[5] or actively, as a result of remedial rehabilitation strategies (ie, exercise).[4]

Functional recovery, in contrast, is a partial or complete improvement in an individual's performance of activities of daily living (ADLs), instrumental ADLs (eg, housekeeping, cooking, washing clothes, paying bills), mobility (eg, transfers, wheelchair use, walking), or communication. The patient **does** better.[4] Because functional recovery is possible even in the complete absence of motor recovery, a summary of the therapeutic scope of rehabilitation, as it applies to stroke, is warranted.[6]

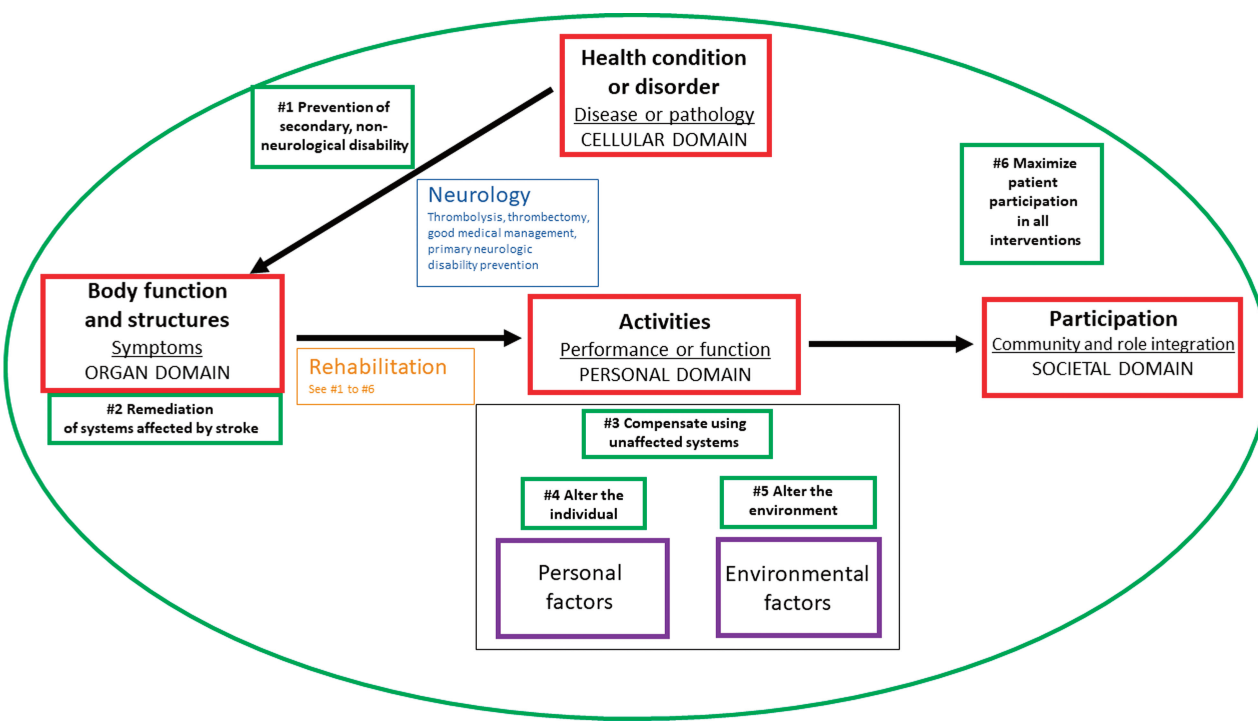

FIGURE 11-1

A conceptual model of stroke rehabilitation interventions in neurology and rehabilitation (based on the International Classification of Functioning, Disability and Health [ICF]). The figure depicts the universe of human health (*green oval*) and its four domains (*red boxes*) as described by the ICF: health condition or disorder (disease or cellular-level domain), body functions and structures (symptoms or organ-level domain), activities (performance or function or person-level domain), and participation (community and role integration of societal domain). These domains are impacted by both environmental and personal factors (*purple boxes*). Most interventions in neurology (*blue box*) occur at the level of treating underlying disease to prevent the subsequent development of symptoms that might eventually cause disability. Rehabilitation intervention (*orange box*) generally occurs after symptoms related to the stroke have already developed and fall into six broad categories (*numbered green boxes*).

Data from DeLisa J, et al[6] and World Health Organization.[9]

Prevention of secondary, non-neurologic disability, such as using range of motion to prevent ankle contractures and minimizing bed rest to prevent deconditioning, is far superior to re-establishing function once lost. Remedial strategies are used to directly treat symptoms resulting from a stroke such as weakness, aphasia, attention deficit, and dysphagia. These remedial strategies are almost always based on exercise or involve methods to augment the effects of exercise and will be discussed in the following sections. Compensatory strategies take advantage of the systems unaffected by stroke such as using the intact, unaffected arm to eat and dress or unaffected leg to help walking. These strategies can immediately increase performance even in the complete absence of symptom resolution. An individual's environment can be modified by using ramps, lowered counter tops, or widened doorways. Likewise, the individual's performance can be modified using upper or lower extremity bracing, functional electrical stimulation,[7] or assistive and mobility devices. To be successful, these approaches all require patient participation and the recognition that rehabilitation is an active process that cannot be done to someone. Rehabilitation therapists and physicians recognize that when motivation, cognition, depression, or anxiety are barriers to learning and patient participation in exercise, those barriers must be addressed using a range of techniques.[6]

All therapeutic strategies are important and necessary in stroke rehabilitation.[8] For patients in the early stages after severe stroke, compensatory techniques are mandatory to maximize independence, minimize burden of care, and facilitate home discharge in an environment of increasingly short hospital stays. Remediation, on the other hand, tends to predominate in mild to moderate stroke and in the outpatient setting.[8] Rehabilitation and neurologic interventions for symptoms and function are best conceptualized within the context of the World Health Organization's International Classification of Functioning, Disability and Health (**FIGURE 11-1**).[9]

Any review of stroke rehabilitation and recovery must necessarily be limited in scope. This article presents the topic in three sections: (1) rehabilitation issues the neurologist will encounter in acute care, (2) a narrative of what occurs during the inpatient and outpatient stroke rehabilitation, and (3) a review of the principles of exercise in stroke rehabilitation and the main strategies to enhance exercise in stroke recovery.

REHABILITATION ISSUES IN ACUTE CARE

In acute care, the rehabilitation team will vary by hospital and by the severity and specific deficits of each patient. The complicated nature of rehabilitation treatment requires the subspecialization of therapists into the disciplines of physical therapy, occupational therapy, and speech-language pathology. The updated American Heart Association/American Stroke Association (AHA/ASA) 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke recommends a "formal assessment" by each of these disciplines before discharge from acute care.[1] In reality, rehabilitation therapists commonly "cross-treat" impairments from other disciplines, especially cognitive and communication deficits that impact learning and participation. For all disciplines, a clear understanding of a patient's baseline level of function is critical given that recurrent stroke and medical comorbidities often contribute to some degree of pre-admission deficits.

KEY POINTS

- **Motor recovery is the partial or complete improvement of an individual's motor symptoms such as weakness, coordination, fine control, or ataxia following a stroke.**

- **Functional recovery is a partial or complete improvement in an individual's performance of activities of daily living, instrumental activities of daily living (eg, housekeeping, cooking, washing clothes, paying bills), mobility (eg, transfers, wheelchair use, walking) or communication.**

The Acute Care Rehabilitation Team

Physical therapists address a patient's mobility, whether the patient is lying in bed, using a wheelchair, or walking. Assessment of safety awareness, fall risk, and the ability to multitask physical and cognitive demands simultaneously all potentially impact discharge disposition. Physical therapists assess if patients need a handheld mobility device, which depends on the extent of hemiparesis, balance deficit, and other presentation specifics such as lateropulsion.[10] Ankle bracing is often deferred to an inpatient rehabilitation facility or the outpatient setting. Careful positioning and frequent repositioning of the arms and trunk by medical staff will minimize soft tissue shortening, shoulder subluxation, and plantarflexion contracture (ie, foot drop).[11] Occupational therapists evaluate the relative contributions of weakness, sensory loss, incoordination, apraxia, neglect, and cognition in performing a range of self-care activities. Safety awareness during transfers, toileting, and standing ADLs are also particularly important to a patient's discharge disposition. Upper extremity loss of joint range at the fingers and wrist can be minimized with a resting splint set in slight wrist extension to help offset the flexor tendon shortening that occurs with hypertonia. Arm support using a pillow or wheelchair tray is always preferred over a sling, which only promotes unwanted adduction and internal rotation tightness at the shoulder.[12] Occupational therapy expertise in visual and cognitive assessment may be diagnostically valuable to the neurologist should the discovery of subtle visual deficits or unexpected cognitive findings occur during higher-level functional activities.

Speech-language pathologists assess and treat communication deficits stemming from impairments in language (aphasia), articulation and phonation (dysarthria), motor planning (verbal apraxia), or from underlying cognitive deficits.[13] These impairments often coexist. The 2021 VERSE (Very Early Rehabilitation for Speech) clinical trial found that a high-dose language intervention (an extra 20 aphasia treatment sessions starting before day 15 and ending before week 4) was no better or worse than usual care.[14] Speech-language pathologists are also key team members in screening for and treating stroke-related swallowing dysfunction.[15] Although the 2018 AHA/ASA guidelines cited insufficient data,[1] a more inclusive 2021 meta-analysis concluded that dysphagia screening in acute stroke care was associated with lower risk of pneumonia, death, and dependency.[16]

Physiatrists (physical medicine and rehabilitation physicians) work closely with therapists to identify factors—whether medical, neurologic, musculoskeletal, or psychological—limiting the mobilization of the patient with acute stroke and to strategize how to effectively overcome these factors. With training grounded in the management of neurologic, cardiopulmonary, and musculoskeletal disability, physiatrists are well positioned to collaborate with neurologists to evaluate, differentiate, and manage primary and secondary disability in both the acute and chronic stages of stroke. Physiatrists also advise neurologists in the complicated process of determining discharge disposition.[17]

Acute Care Interventions

An area of debate is the timing to safely begin mobilization exercises after acute stroke. Early brain plasticity and avoidance of the complications of bed rest and immobility are benefits of early mobilization.[18] However, AVERT (A Very Early

Rehabilitation Trial After Stroke) found that starting mobility training within 24 hours after stroke decreased the odds of achieving a favorable modified Rankin Scale (mRS) score (defined by ≤2 at 3 months) compared with standard care.[18] Stroke progression and 14-day mortality were also more common in the early mobilization group, with the greatest risk in patients aged older than 80 years and in those with intracranial hemorrhage.[19,20] Compared with the usual care group, the treatment group initiated sitting, standing, and walking earlier (18.5 versus 22.4 hours poststroke), more frequently (6.5 versus 3.0 sessions), and for longer (31 versus 10 minutes per day). No differences were found in patients who received or did not receive thrombolysis therapy, and data suggested that while increased exercise intensity (more minutes) may be detrimental to outcome, increased frequency (more sessions) may actually be beneficial.[19] The AMOBES (Active Mobility Very Early After Stroke) trial found no benefit to high-intensity (45 versus 20 minutes) daily physical therapy initiated within 72 hours of stroke, but was likely grossly underpowered, and the sample was over-represented by participants with severe stroke.[21] Although further research is clearly required, the 2018 AHA/ASA guidelines recommend that specialized acute stroke units incorporate rehabilitation into their care and discourage mobilization prior to 24 hours poststroke, but otherwise make only very general recommendations.[1] Until more clinically useful early mobilization guidelines are widely available,[20] acute care rehabilitation goals should include safely initiating mobilization; monitoring the stability and functional impact of motor, sensory, language, and cognitive deficits; preventing musculoskeletal, pulmonary, and skin complications; and preparing the patient and family for the next phase of rehabilitation, whether that be in an inpatient or outpatient setting.[19]

KEY POINT

- Although further research is clearly required, the 2018 American Heart Association/American Stroke Association guidelines recommend that specialized acute stroke units "incorporate rehabilitation" into their care and discourage mobilization prior to 24 hours poststroke, but otherwise make only very general recommendations.

The pharmacologic enhancement of recovery from stroke (see Exercise Approaches section) has received much attention[22-24]; however, from the early animal studies by Feeney and colleagues,[25] certain medication classes have also been considered detrimental to recovery.[26-29] On the basis of both clinical and animal data, detrimental classes commonly include benzodiazepines,[28,30] first-generation antipsychotic medications,[25,28] centrally acting antihypertensive agents,[28] and the antiepileptic agents phenytoin and phenobarbital.[31,32] Avoiding these medication classes during acute stroke care is especially critical given the greatest impact is likely to occur early after stroke presentation and in those with more severe injury.[26,31]

Outcome prediction after stroke and the natural history of stroke are somewhat related topics, and both are of great importance to patients and society.[33] It is generally accepted that most natural motor recovery occurs during the first 3 to 6 months poststroke and then the patient achieves a plateau.[26] Some authors maintain that motor recovery can continue up to a year.[34] Defining a plateau at the functional or activity level is especially confounded by the ceiling effects of assessment scales, definitions of "clinically significant," and important change at the individual level not captured when analyzing mean change across groups.[35] A variety of methods (clinical, technologic, and imaging)[36] have been used in the first week poststroke to predict recovery at both the impairment and activity levels.[37] One of the best-known methods is the Predicting Recovery Potential (PREP) algorithm, which combines clinical assessment of shoulder abduction and finger extension along with neuroimaging and neurophysiologic assessment to predict Action Research Arm Test scores at 12 weeks poststroke.[38]

The widespread use of electronic health records makes a recently described computerized method using only repeated shoulder abduction and finger extension assessments to predict 6-month Action Research Arm Test scores particularly appealing.[33] This is usually the Fugl-Meyer Assessment, with scores ranging from 0 to 66 for the upper extremity. For example, if the initial Fugl-Meyer Assessment in acute care is 32/66, then the patient can be expected to gain 70% of the remaining points on the scale (about 24) and achieve a maximum score of about 56 within 3 to 6 months. However, the calculation is accurate in only about 70% of people with stroke (the so-called "fitters").[39] Imaging has been suggested to help distinguish "fitters" from "nonfitters."[40] Although appealing, the theory has been widely criticized based on mathematical coupling,[41,42] poor applicability in severe impairment,[43] significant sensitivity to ceiling effects,[41,42] and poor discrimination with quality-of-life measures.[44]

Inpatient Rehabilitation Referral

Whether to transfer to inpatient rehabilitation is among the final decisions for a patient with moderate or severe stroke on the acute neurology service. Occurring a mean of only 9 days after admission to acute care in the United States,[45] transfer to rehabilitation can be complicated by confusion, contradiction, and inconsistency because of an uneven availability of acute rehabilitation beds, variable insurance criteria, complicated referral patterns, and a myriad of federal regulations for these diagnosis-related group–exempt rehabilitation units.[17] Although patient preferences should be taken into consideration, neurologists should clearly understand and educate their patients on the differences in care provided by an inpatient rehabilitation facility and skilled nursing facility or "subacute" rehabilitation unit. In an inpatient rehabilitation facility, federal oversight guarantees an intensity of rehabilitation therapy, nursing staffing, physician oversight, and team coordination that rarely exists in a skilled nursing facility. Using sophisticated statistical modeling to minimize referral biases, a comparison of more than 33,000 inpatient rehabilitation facility and 66,000 skilled nursing facility Medicare beneficiaries undergoing stroke rehabilitation found double the gains in self-care and mobility among the inpatient rehabilitation facility group compared with the skilled nursing facility group.[46] The difference in self-care was the equivalent to that of requiring maximal assistance from another person versus needing only another person present but no physical assistance (ie, needing continued institutionalization among the skilled nursing facility group versus ready-for-home discharge for the inpatient rehabilitation facility group).[46] Other studies have underscored the value of organized inpatient stroke rehabilitation in maximizing functional status, minimizing medical complications, decreasing 30-day readmission rates, and reducing mortality.[47-49] The 2016 AHA/ASA Guidelines for Adult Stroke Rehabilitation and Recovery state that, when available, all patients with stroke who cannot return home should be evaluated for an inpatient rehabilitation facility at the conclusion of an acute hospitalization.[50] In 2021, the AHA/ASA also put forth an acute care stroke rehabilitation performance measure stating that "[p]eople with stroke who qualify for, would benefit from, and have geographic access to [inpatient rehabilitation facility] IRF care should receive acute inpatient rehabilitation in an IRF."[51] Based on evidence and guidelines, it is appropriate for the neurologist to advocate for their patients with stroke who cannot return home to receive inpatient rehabilitation facility assessments. Admission to a skilled nursing facility, without inpatient rehabilitation facility consideration, only for the sake of expediency to decrease acute care lengths of stay, to maintain historical referral patterns, or to prevent "bleed" outside of a constituent health care system should be viewed as incompatible with best practices. That said, the intensity of an inpatient rehabilitation facility naturally excludes some patients with stroke who are medically or cognitively unable to participate. These individuals are more suitable for skilled nursing facility–based rehabilitation programs and include patients with concomitant neurologic disease like dementia or moderate Parkinson disease or significant medical issues such as poorly controlled congestive heart failure or pulmonary disease, active cancer, advanced bilateral lower extremity osteoarthritis, or peripheral vascular disease in the setting of poor surgical risk.

In summary, rehabilitation plays an increasingly important role during the first several days following a stroke as a patient becomes medically and neurologically stable. A variety of rehabilitation professionals will use both remedial and compensatory strategies to gradually mobilize a patient and help the neurologist to monitor motor and functional stability and recovery. The neurologist can avoid detrimental medications that may slow recovery and should feel confident in advocating for an inpatient rehabilitation facility evaluation before discharge for patients who cannot return home. At the conclusion of acute care, about 44% of patients with stroke will be discharged to some type of inpatient rehabilitation and another 12% will be discharged home with home care.[51] Earlier initiation of transfer to inpatient rehabilitation, when possible, is likely beneficial.[52] In addition, many patients with stroke will participate in an outpatient rehabilitation program on discharge from acute care or after an inpatient rehabilitation stay. Although acute stroke care has been far better developed than post–acute stroke care in the United States,[53] patients with stroke can expect to enter a new phase of treatment and recovery postdischarge that will potentially last several months and introduce them to new rehabilitation providers and settings (CASE 11-1).

KEY POINT

- **Admission to a skilled nursing facility, without inpatient rehabilitation facility consideration, for the sole purpose of decreasing acute care lengths of stay, maintaining historical referral patterns, or preventing "bleed" outside of a constituent health care system should be viewed as incompatible with best practices.**

INPATIENT AND OUTPATIENT REHABILITATION

Perhaps no better manifestation of "health care team" exists than what occurs during an inpatient rehabilitation facility stay. Lead by a physiatrist (or similarly qualified physician), a group of up to seven disciplines provides highly coordinated medical, physical, and psychosocial care over 3 to 4 hours of therapy and 20 to 21 hours of nursing care, 6 days a week for 1 to 3 weeks. Rehabilitation nursing serves as the glue that holds together the inpatient rehabilitation facility experience. These nurses, many of whom are certified rehabilitation registered nurses, have additional training and expertise in recognizing cognitive and language impairments and in managing and preventing bowel, bladder, and skin complications. In addition to providing traditional medical nursing, they integrate ADLs and toileting, transfer, and mobility skills learned during rehabilitation therapies into the remainder of the day. Physical and occupational therapists and speech-language pathologists build on the treatments discussed above in the acute care setting. Greater emphasis is placed on improving activity endurance, strengthening, and cognitive task demands. Far more time and emphasis are placed on the treatment of language disorders at an inpatient rehabilitation facility compared with acute care. Likewise, dysphagia treatment starts in earnest, including muscle strengthening exercises, peripheral stimulation, and compensatory techniques.[54] Nutritionists help track caloric needs in the setting of potential dysphagia, depression, chronic illness, and other conditions impacting intake and appetite. Therapeutic recreation provides structured treatment for cognitive, motor, and language impairments during social interactions disguised as enjoyable "nonmedical" activities. Screening by neuropsychologists not only delineates the scope of cognitive deficits, but also provides guidance for therapists in areas of cognitive weakness for remedial therapy and strengths to leverage compensatory strategies. Social work assumes dual roles of logistics for discharge planning and psychological counseling for patients and their families at, perhaps, one of the most stressful times in their lives.

The medical philosophy at an inpatient rehabilitation facility is quite different from the rest of the hospital. Referring and consulting physicians are sometimes perplexed that procedures and conditions easily accomplished and treated on a medical floor are challenging at an inpatient rehabilitation facility. Succinctly put, patients are admitted to an inpatient rehabilitation facility primarily to be mobilized rather than receive medical care (although a great deal of medical care is typically provided). Any condition, development, or workup detracting from that mobilization must be addressed off the unit. If the patient cannot move (ie,

CASE 11-1

A 65-year-old man presented to the emergency department with a blood pressure of 190/140 mm Hg, a severe left hemiparesis, and moderate dysarthria. He had woken up that morning with left-sided weakness but decided to "wait it out" until lunch, when his speech began slurring. He had previously been independent. MRI showed a large right middle cerebral artery infarction, and he was past the window for thrombolysis.

The patient was admitted for blood pressure control and evaluation. A swallowing screen performed by a speech-language pathologist indicated silent aspiration, and a modified diet with thickened liquids was ordered. Physical and occupational therapies were initiated after 24 hours, revealing that moderate assistance was required for dressing, toileting, transfers, and walking, which was complicated by neglect and poor safety awareness. Inpatient rehabilitation was recommended and the patient was transferred to an inpatient rehabilitation facility. At 5 days poststroke, progress was initially limited by shoulder pain, managed by an occupational therapist with taping, and by depression, treated by a physiatrist with pharmacotherapy. The speech-language pathologist focused on exercises to strengthen muscles for both swallowing and articulation, with good results. Robotics were used to enhance lower extremity exercise and functional electrical stimulation was used to enhance upper extremity exercise. After 16 days, the patient was discharged home from inpatient rehabilitation able to walk with a cane and supervision and needed assistance only for lower extremity dressing. He was on a regular diet and liquids and speech intelligibility was 90%.

The patient initiated an outpatient rehabilitation program 3 days a week with a speech-language pathologist, physical therapist, and

attend and participate in rehabilitation therapies), they cannot remain at an inpatient rehabilitation facility; therefore, in addition to leading the rehabilitation team, the essential task of the attending physiatrist is to ensure that patients at the inpatient rehabilitation facility are medically stable and free of pain and mood disturbances or other issues so that they can participate in therapy, remain on the unit, and benefit from the rehabilitation experience.

Most patients will see at least some, if not substantial, functional progress during a typical 1- to 3-week inpatient rehabilitation facility stay. Patients and families should understand that rehabilitation admissions are relatively short. In the United States in 2021, the mean length of stay at inpatient rehabilitation facilities for patients with stroke was 14.1 days.[45] Patients in an inpatient rehabilitation facility will probably see more progress and independence with walking and mobility than with ADLs and self-care. An assistive device for mobility may still be required at discharge (or even hands-on assistance of a family member), but most patients will be able to get around in their home. In their 2020 study, Moore and colleagues[55] implemented a high-intensity stepping protocol during inpatient rehabilitation. By increasing the total number of daily steps by 32% and achieving 70% to 85% of the maximum heart rate, the

occupational therapist, who used transcranial direct current stimulation in his treatment program. A left ankle-foot orthosis was prescribed to facilitate walking. Outside of therapy sessions, the patient joined a walking group to increase cardiovascular fitness. Although the recovery of his strength was not complete, he was independent in walking without an assistive device (although slow) and independent in all activities of daily living (primarily with the right hand using the left hand as an assist).

COMMENT

This case demonstrates several key aspects of stroke rehabilitation and recovery. Prevention of further disability is illustrated by dysphagia screening to minimize aspiration pneumonia. Mobilization should be initiated only after 24 to 48 hours poststroke with safety awareness being a priority, which is important in discharge planning. All patients with stroke who cannot return home should be evaluated for an inpatient rehabilitation facility. Stroke recovery is dependent on exercise, and exercise is an active process contingent on participation. Pain, mood disorders, and medical instability are frequently barriers to participation and must be addressed when they occur. A variety of strategies were used during inpatient and outpatient rehabilitation to enhance poststroke exercise in his care including robotics and transcranial direct current stimulation. Although this patient had an incomplete motor recovery, he did have a nearly complete functional recovery.

high-intensity group achieved faster gait speeds and better balance and endurance at inpatient rehabilitation facility discharge. Likewise, another 2020 study showed increased stepping activity during an inpatient rehabilitation facility stay led to better outcomes even a year later.[56] The degree of independence achieved in ADLs is more variable and depends on the severity of impairment, side of weakness, and hand dominance. A reasonable degree of independence can be expected, with mild weakness in the dominant arm or any degree of weakness in the nondominant arm. An accurate prediction is elusive because patterns of proximal and distal weakness, the degree of sensory deficits, coordination, apraxia, and cognitive and communication status all play a role in the final level of independence. Gains made during the inpatient rehabilitation facility stay are predictive of both short-term disability[57] and long-term mortality.[58] In about 10% of cases, a patient with stroke will be discharged from an inpatient rehabilitation facility to a skilled nursing facility.[45] Reasons for this include the family being unable to provide care at home or the patient awaiting return of bowel or bladder continence, needing cognitive supervision despite good physical recovery, or having a specific physical barrier at home (eg, bathroom on the second floor or a three-story or four-story walk-up apartment in urban areas.)

Most patients discharged from an inpatient rehabilitation facility to home will continue rehabilitation in an outpatient setting. This could include one to three therapies two to three times a week for a few weeks or a few months. As detailed in the following section on exercise approaches, this likely represents a gross underdosing of therapy.[59-61] The program will likely continue strengthening and improvement of fine motor coordination, but cardiovascular conditioning and high-level balance training will also become a greater focus. Aerobic conditioning is important not only from a recovery standpoint, but also from a secondary stroke prevention perspective.[62,63] Patients will also be expected to carry out a home exercise program under the supervision of their therapist. Most outpatient therapy will be remedial. A long-term challenge for any person with stroke is actually using their affected extremities, especially when the nondominant upper extremity is involved. While understandable (ie, using a weak, possibly insensate, uncoordinated hand can be slow, unsightly, embarrassing, and frustrating), this barrier of “learned nonuse,” as posited by Taub,[64] becomes a major obstacle to the patient and rehabilitation team. Potential function in an affected limb lies fallow as a patient gradually “learns” it is easier and more efficient to use the unaffected limb. The rehabilitation process itself may inadvertently contribute to learned nonuse if compensation is overly emphasized relative to remediation.

A variety of other rehabilitation-related events may occur in the outpatient setting. The use of an ankle-foot orthosis or other brace may occur at this time, depending on the relative presentation of anterior leg dorsiflexion weakness versus posterior leg plantarflexion spasticity. Botulinum toxin treatment can be considered in the latter case.[65] For individuals with reasonable cognitive ability whose mobility has not improved to the point of community ambulation, an assessment for a scooter or power mobility may be appropriate. In addition to physiatry, physician referrals to urology for bladder management, psychiatry for severe depression or anxiety, and orthopedic surgery for upper or lower extremity tendon releases may be appropriate if there are intractable hygiene issues or unmet function goals.

EXERCISE-BASED STRATEGIES TO ENHANCE MOTOR RECOVERY AFTER STROKE

Much of the rehabilitation experience—whether inpatient, outpatient, or at home—as it relates to motor recovery after acute care discharge revolves around exercise. Some of the recovery following stroke occurs passively, without exercise, with the resolution of acute edema and diaschisis and normalization of cell properties, ion levels, and neurotransmitters in the immediate vicinity of the infarction.[5,66] The physiologic basis of motor recovery resulting from active exercise is beyond the scope of this discussion[66] but includes axonal sprouting,[67] long-term potentiation, so-called "hebbian plasticity,"[66] unmasking of latent tracts,[5] and cellular proliferation zones.[68] In 2019, Maier and colleagues[69] outlined 15 principles of neurorehabilitation after stroke (TABLE 11-1). Although all are important, two principles seem to be the most consistently cited as defining an effective exercise program following stroke: task-specific exercise and repetition or mass practice.[26,69,70] For a hand to recover, muscles of the hand specifically must be repeatedly exercised. For walking to improve, the muscles involved in walking must be exercised extensively. Other important aspects of exercise after stroke include variability (both within and between sessions), increasing difficulty, simultaneous sensory stimulation (visual, auditory, haptic), and explicit feedback on performance.[69] If the characteristics and content of exercise constitute the science of stroke rehabilitation, equally important must be the art of rehabilitation as practiced by an outstanding therapist. Key is a therapist's ability to tailor exercises to individual patients at a level that is challenging but not overly frustrating; to provide assistance when needed, but only just enough to finish that repetition; to choose short-term and long-term goals that progressively achieve the next functional level but not too aggressively or easily; and to provide constant encouragement and positive feedback.[69] This personalized interaction between patient and rehabilitation therapist is simply the secret ingredient that may never be fully elucidated or accurately or consistently replicated in any clinical trial of motor recovery following stroke.

As suggested below, the requirement of active engagement in exercise following stroke inherently carries a presumption of participation. The management of this aspect of stroke rehabilitation is overlooked and underappreciated. In the inpatient setting, medical complications like orthostatic hypotension, underlying cardiac and pulmonary disease, and preventable complications like deep venous thrombosis and infections of the lungs and bladder often limit participation. It falls to the physician on the team to prevent and treat these conditions. In both the inpatient and outpatient realms, any type of pain must be diagnosed and treated promptly with a regimen having the least possible impact on cognition. If depression, anxiety, or poor initiation limit active participation, motivational techniques, counseling, or medications must be considered to maximize participation as quickly as possible. Frustration, anger, inadequate coping skills, and poor adjustment to disability are other factors that can undermine participation on a given day or over a longer time. Close communication, coordination, and management among therapists and physicians is required to identify and minimize the impact on progress.

Exercise Approaches

Regardless of whether the upper[2] or lower limb is predominantly affected,[70] few patients with stroke experience a full recovery. Significant questions remain

KEY POINTS

- In addition to leading the rehabilitation team, the essential task of the attending physiatrist is to ensure that patients at the inpatient rehabilitation facility are medically stable and free of pain and mood or other issues to the degree that they can participate in therapy, remain on the unit, and benefit from the rehabilitation experience.
- Most patients discharged from an inpatient rehabilitation facility to home will continue rehabilitation in an outpatient setting. This could include one to three therapies, two to three times a week from a few weeks to a few months, which likely represents a gross underdosing of therapy.
- If the characteristics and content of exercise constitute the "science of stroke rehabilitation," equally important must be the "art of rehabilitation" as practiced by an outstanding therapist.
- Significant questions remain surrounding the ideal exercise protocol following stroke, despite numerous large clinical trials over the past 2 decades.

surrounding the ideal exercise protocol following stroke, despite numerous large clinical trials over the past 2 decades. As mentioned previously, the AVERT Trial[18] demonstrated that exercise delivered too soon after stroke can be detrimental. The VECTORS (Very Early Constraint-Induced Movement during Stroke Rehabilitation) trial[71] compared high-intensity constraint-induced motor therapy to dose-matched constraint-induced motor therapy and usual care in an inpatient rehabilitation facility setting. While no difference was found between the usual care and dose-matched constraint-induced motor therapy groups, the high-intensity constraint-induced motor therapy group had a worse outcome, demonstrating that more exercise is not always better. The 2021 CPASS (Critical Period After Stroke Study) provided an additional 20 hours of therapy at three

TABLE 11-1 **Fifteen Principles of Neurorehabilitation Exercise[a,b]**

Neurorehabilitation Exercise Principle	Definition	Examples
Massed practice (repetitive practice)	Exercise episodes with very brief to no rest breaks; prolonged and repeated use of the more affected limb	Assuring that an adequate number of repetitions of a given movement are implemented over a course of treatment to achieve a given goal
Spaced practice	Training is structured to provide rest break between repetitions or sessions	The use of objective or subjective assessments or a predetermined schedule to provide rest breaks during a therapy session
Task-specific practice	Conditions during training should match the conditions during testing (or performance)	Aligning an exercise program with the most-impaired limb or muscle groups, or with the goal of a specific functional task
Dosage	Multiple dimensions: number of training hours per time period, frequency and duration of training sessions, intensity	Increasing the intensity, frequency, or complexity of exercises over time to increase difficulty or variability over time
Goal-oriented practice	Motor training to achieve a goal (eg, combing one's hair) is more effective than training the individual muscles and movements required to complete the task	Therapists negotiating reasonable and attainable functional goals for an individual session or over the course of several sessions
Variable practice	Providing variable tasks (or intensity) within (and between) training session(s)	A therapist randomizing the types, difficulty, and nature of exercise during a given session and between sessions over time
Increasing difficulty	Increasing the difficulty of a task in relationship to the skill of the performer	"Shaping" in constraint-induced motor therapy; increasing resistance or repetitions of exercises over time; integrating individual limb movement into more complex activities of daily living
Multisensory stimulation	The perception and integration of one or more senses during the performance of an action	Haptic, visual, and auditory stimuli utilized in upper extremity robotics and brain-computer interfaces; use of a mirror to visualize movement during therapy

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different time periods during the first year after stroke compared with a control.[72] The additional dose delivered 2 to 3 months following stroke yielded greater gains at 1 year compared with doses delivered earlier than 30 days, after 6 months, or in the control group.

Therefore, the timing of exercise after stroke also matters. Over the past 2 decades, several variations on a standard poststroke exercise program have been examined. One of the few proven treatments for motor recovery following stroke is constraint-induced motor therapy. Designed to thwart learned nonuse,[64] classic constraint-induced motor therapy forces a huge amount of use in the affected upper extremity over a short period of time (about 2 weeks). The EXCITE trial demonstrated that, compared with usual and customary care,

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Neurorehabilitation Exercise Principle	Definition	Examples
Rhythmic cueing	Synchronizing (training) movements to rhythmic patterns	Use of a metronome to initiate or increase speed to a repetitive movement; use of regular tones to facilitate gait in Parkinson disease or for persons with stroke on a treadmill
Explicit feedback or knowledge of results	Verbal, terminal, or augmented feedback about goal achievement	A therapist providing detailed feedback to a participant regarding the quality or accuracy of a movement or task
Implicit feedback or knowledge of performance	Verbal descriptions, demonstrations, or replay of recordings of movement execution as feedback	Biofeedback; use of sound or visual colors when an action crosses a minimal threshold; use of virtual reality technology
Modulate effector selection	The tendency to overuse the nonimpacted extremity while underusing the impacted extremity	Constraint-induced motor therapy; overutilizing compensatory over remedial strategies
Action observation or embodied practice	Observing the movement of another individual to improve the participant's movement	A therapist demonstrating to a participant a given action or task prior to actual attempt
Mental practice or mental imagery	Mentally simulating actions without overt behavior of the movement	Participant imagining a given movement prior to or independently of an actual exercise in therapy
Social interaction	Behavior in which the participant's actions are both a response to and a stimulus for the counterpart's behavior	Friends and family encouraging both training and the goal of independence; development of a therapeutic alliance between a participant and therapist; recovery in an enriched environment

[a] Data from Maier M, et al, Front Syst Neurosci.[69]

[b] In practice, there is overlap among these 15 principles and research has often not been able to isolate a specific principle for study. Some of the evidence for these principles was derived from the study of healthy individuals. The schema provides a framework for the description and understanding of exercise (and experience) after stroke, and other neurologic conditions or injuries.

constraint-induced motor therapy led to significant gains in the use of the affected arm in 222 participants 3 to 12 months poststroke and that gains lasted 2 years after the trial.[73,74] Despite this, constraint-induced motor therapy is labor intensive (6 hours a day, 5 days a week, for 2 weeks), expensive, logistically challenging, and very frustrating for the patient; therefore, modified constraint-induced motor therapy designs have been proposed[75] but not widely implemented. Among patients with voluntary finger extension, modified constraint-induced motor therapies initiated about a week poststroke and lasting 5 weeks were beneficial for up to 12 weeks but were not sustained at 26 weeks.[76] The ICARE (Interdisciplinary Comprehensive Arm Rehab Evaluation) trial compared three rehabilitation approaches: a structured, task-oriented, upper extremity training program of 30 hours over 10 weeks; a dose-matched occupational therapy program; and monitoring of those among 361 participants who were a mean of 46 days poststroke with moderate impairment.[77] No significant differences were found in the primary outcome measures among the three groups.

Recent studies using much higher doses of exercise have reported more favorable results. The Queen Square program[60] provided 90 hours of therapy over 3 weeks in 224 participants with chronic stroke (median time poststroke was 18 months) with significant gains in impairment and activity lasting 6 months after the trial. Combining these data with the less intense therapy provided in the Rehabilitation Gaming System dataset, Ballester and colleagues[61] retrospectively reported greater Fugl-Meyer Assessment gains with greater intensity rehabilitation and when initiated earlier following stroke. A 2019 trial by Cramer and colleagues[59] found that among 124 participants who were 4 to 36 weeks poststroke and who were randomly assigned to 36 sessions (70 minutes each over 6 to 8 weeks), therapy delivered via telerehabilitation was noninferior to that delivered in clinic. Collectively, these studies suggest current clinical practice significantly underdoses upper limb rehabilitation following stroke. Regarding the lower extremities, the LEAPS (Locomotor Experience Applied Post Stroke) trial compared 54 hours of body weight–supported treadmill training over 12 to 16 weeks either 2 or 6 months poststroke to standard home physical therapy 2 months poststroke.[78] Again, no difference was seen between the three groups regarding walking speed, motor recovery, balance, or quality of life at 1 year poststroke. Like the upper extremity, lower extremity and ambulatory strategies focus on increased stepping (with or without orthotics) and higher exercise intensities and, possibly, the use of mechanical devices in more severe impairment (see the following section on robotics).[70] Other recent novel variations on poststroke exercise with favorable initial results include mirror therapy[79] and virtual reality.[80]

Given the challenges, expense, and logistics of providing ever greater doses of exercise, identifying strategies to augment the effect of exercise on recovery after stroke is desirable. This perhaps has been the most active area of research in stroke recovery, ranging from the acute through the chronic phases. And yet, what has been broadly consistent since the time of Feeney and colleagues'[25] animal drug studies 40 years ago is that active exercise is still the crucial component and the active ingredient in stroke recovery. With only a few notable exceptions,[81] technologic, mechanical, or biological strategies have been implemented as an adjunct to active exercise. Categories of strategies to augment the impact of exercise include pharmacologic enhancement, robotics, functional electrical stimulation, neuromodulation (invasion and noninvasive), and others, including regenerative techniques.[82]

Pharmacologic Approaches

The search for a "magic pill" to cure motor deficits after stroke is appealing but has remained elusive. The mechanisms by which medications facilitate recovery could include changes at a physiologic level by enhancing plasticity[82] resulting from exercise or at a behavioral level by facilitating better attention or motivation resulting in better participation or enhanced mass practice.[24] Among the older studies, initial reports of dopamine agonists such as amphetamine and levodopa were encouraging, but subsequent trials failed to replicate the initial results.[22,24] In 2019, the large, well-designed randomized clinical trial of co-careldopa during early rehabilitation (DARS [Dopamine Augmented Rehabilitation in Stroke]) failed to demonstrate an impact on independent walking or most secondary outcomes.[83] Two small studies reported mixed results with the acetylcholinesterase inhibitor donepezil.[24] Great enthusiasm was generated by the 2011 FLAME (Fluoxetine for Motor Recovery After Acute Ischaemic Stroke) trial, which demonstrated impressive upper and lower extremity motor gains associated with the selective serotonin reuptake inhibitor (SSRI) fluoxetine.[84] This optimism has been dispelled over the past few years with the subsequent publication of three very large clinical trials: AFFINITY (Assessment oF FluoxetINe In sTroke recoverY),[85] EFFECTS (Efficacy oF Fluoxetine-a randomisEd Controlled Trial in Stroke),[86] and FOCUS (Effects of Fluoxetine on Functional Outcomes After Acute Stroke)[87]; all three studies failed to demonstrate a difference between the fluoxetine and placebo groups on the mRS at 6 months and two of the three studies failed at 12 months. Solid criticisms of these trials include the failure to couple medications with active exercise[3] and reservations in using the mRS as a primary outcome measure.[3,88] Finally, a 2020 large randomized clinical trial of S44819 (a γ-aminobutyric acid [GABA] α-5 antagonist) in participants 2 to 6 days poststroke revealed no therapeutic effect between placebo and two different doses on mRS at 90 days.[89] Thus, to date no pharmacologic agents in well-designed randomized clinical trials have clearly demonstrated enhanced motor recovery after stroke.

Robotics

Robotics have been implemented in stroke recovery for nearly 2 decades for both the upper and lower extremities.[90] Robots can be either wearable (exoskeletons) or end effectors (ie, essentially used as a piece of exercise equipment).[91] As end effectors, advantages include a huge increase in the number of repetitions and better participation by using enjoyable games and visual, auditory, and haptic stimulation. Some devices also collect objective kinematic data and other parameters to track progress. On the downside, these devices tend to be very expensive.[90] The clinical data on robotics are underwhelming, with most studies and meta-analyses finding their efficacy no better than dose-matched usual care. The 2019 RATULS (Robot Assisted Training for the Upper Limb After Stroke) trial[92] did not find upper extremity robotics treatment better than dose-matched traditional rehabilitation therapy or usual care. Two other recent upper extremity robotics clinical trials reported similar findings.[93,94] There may be an advantage to lower extremity robotics in patients with severe stroke.[70,91] Clinical data on the use of exoskeleton devices in stroke are scant, and their roles are unknown at this

KEY POINTS

- **Given the challenges, expense, and logistics of providing ever greater doses of exercise, identifying strategies to augment the effect of exercise on recovery after stroke is desirable.**
- **To date no pharmacologic agents in well-designed randomized clinical trials have clearly demonstrated enhanced motor recovery after stroke.**

time.[95,96] Despite an underwhelming track record, upper and lower extremity robotics and exoskeletal devices are commonly offered at larger rehabilitation centers.

Functional Electrical Stimulation

Neuromuscular stimulation uses electricity to facilitate the peripheral contraction of a paralyzed muscle that is still innervated, as is the case in an upper motor neuron lesion like stroke.[97] A variety of systems are available (eg, transcutaneous, percutaneous, and implantable) that have been used to treat spasticity and muscle atrophy. Some evidence suggests that neuromuscular stimulation enhances motor recovery, termed a *therapeutic effect*.[7,97,98] More recently, implantable systems have been used to treat poststroke shoulder pain, as well.[99] Functional electrical stimulation is a subcategory of neuromuscular stimulation in which the stimulation is manipulated to produce purposeful muscle movements. Although this can be applied in the arm, functional electrical stimulation is more often used in the leg to dorsiflex the ankle in the swing phase of gait to compensate for foot drop after stroke, also known as the *training effect* or *orthotic effect*.[7] Compared with an ankle-foot orthosis, lower extremity functional electrical stimulation may decrease the physiologic cost of gait (based on resting and working heart rate and walking speed) but does not improve gait speed.[100] A recent meta-analysis found moderate evidence that functional electrical stimulation results in improvements at an activity level, more so in the arm than in the leg.[101]

Neuromodulation

Neuromodulation alters cortical activity in the brain with the goal of augmenting the effect of exercise to enhance recovery from stroke. Modulation can be either excitatory or inhibitory, depending on the target, and is more or less spatially focused, depending on the delivery system.[102] The stimulation can be provided invasively (ie, implanted vagus nerve stimulation [VNS] or epidural stimulation) or noninvasively (ie, repetitive transcranial magnetic stimulation and transcranial direct current stimulation). An encouraging clinical trial from 2021 used VNS, a surgically implanted device similar to that used in epilepsy, which provides a nonlocalized release of neurotransmitters in the central nervous system.[103] Dawson and colleagues[103] had therapists use a hand-held device to activate the VNS device while patients performed active upper extremity exercise. Among 108 participants about 3 years poststroke, VNS or sham stimulation was combined with 27 hours of occupational therapy over 6 weeks. The VNS group was about twice as likely to achieve a clinically meaningful gain on Fugl-Meyer Assessment and three times as likely to do so on the Wolf Motor Function Test compared with the control group. Adverse events were mild and expected. A 2021 meta-analysis, which included the 2021 VNS trial mentioned above and noninvasive devices, confirmed that VNS is effective for facilitating recovery of upper extremity function.[104] Other invasive options include epidural stimulation. The 2016 EVEREST trial[105] neurosurgically implanted epidural stimulation arrays over the motor cortex in 94 participants (mean 5 years poststroke) followed by 6 weeks of therapy. Although no difference was found in the primary endpoint between the experimental and control groups, participants who responded to motor stimulation testing at baseline appeared to do better.

Repetitive transcranial magnetic stimulation uses a noninvasive, magnetic field to alter excitability of brain tissue with good spatial accuracy.[102] The technology can be used to either stimulate or inhibit cortical activity, usually *before* exercise is introduced. The upper extremity, not the lower extremity, is the usual target owing to its relatively more superficial and accessible location on the motor homunculus. In a meta-analysis of studies prior to 2018, He and colleagues[106] found low-frequency repetitive transcranial magnetic stimulation had a positive effect on motor recovery for grip strength and lower limb as measured by the Fugl-Meyer Assessment. Not included in that analysis, however, was the 2018 trial NICHE (Navigated Inhibitory rTMS to Contralesional Hemisphere Trial).[107] In 197 participants 3 to 12 months poststroke, NICHE failed to demonstrate an upper extremity effect of low-frequency repetitive transcranial magnetic stimulation administered to the unaffected cortex prior to 18, 1-hour therapy sessions over 6 weeks. No differences were found for the Fugl-Meyer Assessment or any secondary outcome between the repetitive transcranial magnetic stimulation and sham groups. Conversely, a 2021 systematic review concluded that high-frequency repetitive transcranial magnetic stimulation to the ipsilateral cortex results in decreased upper extremity impairment.[108] This technology has also been used in the treatment of aphasia[109] and other impairments.[102]

Transcranial direct current stimulation delivers a small electrical current (1 mA to 2 mA) through the scalp and skull to the cortex, altering the excitability of brain tissue.[102] As opposed to repetitive transcranial magnetic stimulation, transcranial direct current stimulation is generally applied during exercise or activity and has less spatial accuracy. Although transcranial direct current stimulation is more limited in its ability to penetrate the deeper cerebral structures, it is technically easier and somewhat safer to use than transcranial magnetic stimulation and therefore has been somewhat more widely implemented in a clinical setting. A 2021 meta-analysis found modest evidence that transcranial direct current stimulation improved ADLs, but not limb strength, neglect, or cognition,[110] and it had variable effects on walking and ambulation after stroke.[111] The results appear to be a bit more promising when function is used as the outcome of the meta-analysis.[112]

Miscellaneous Strategies

Several regenerative approaches have been used over the past several years to enhance stroke recovery,[2,81,113] with several trials ongoing.[81] All regenerative approaches remain investigational only. Regenerative cell lines have been derived from various sources (eg, mesenchymal, hemopoietic) and delivered intravenously, intraarterially, and intracranially.[81] Results have reflected good safety and emerging evidence of efficacy.[114,115] Unlike the other strategies discussed above, many clinical trials examining stem cells did not include formal exercise therapy as part of the protocols. The CARS (Cerebrolysin and Recovery After Stroke) trial was a randomized clinical trial that studied a porcine neuropeptide, which was started 24 to 72 hours after stroke in 208 participants and continued daily for 3 weeks along with a standard inpatient rehabilitation program.[116] The CARS trial found a beneficial effect at the impairment and global outcomes levels with a favorable safely profile. Growth factors have been examined, with granulocyte colony-stimulating factor perhaps being the most promising, but with no clear positive results to date.[82] Other emerging

KEY POINTS

- **Despite an underwhelming track record, upper and lower extremity robotics and exoskeletal devices are commonly offered at larger rehabilitation centers.**

- **Compared to an ankle-foot orthosis, lower extremity functional electrical stimulation may decrease the physiologic cost of gait (based on resting and working heart rate and walking speed) but does not improve gait speed.**

- **The vagus nerve stimulation group in one trial was about twice as likely to achieve a clinically meaningful gain on the Fugl-Meyer Assessment and 3 times as likely to improve on the Wolf Motor Function Test compared with the control group.**

KEY POINT

- **Defining the optimal nature, characteristics, intensity, and timing of a patient's participation in task-specific and repetitious exercise to maximize motor recovery constitutes the fundamental challenge in stroke rehabilitation.**

strategies include the use of monoclonal antibodies[2] and brain-computer interfaces.[82,90]

In summary, the past decade has shed light on a few promising strategies to enhance motor recovery resulting from exercise following stroke. The underlying reasons for numerous recent unsuccessful trials in this area have been eloquently reviewed and discussed by Stinear and colleagues.[3] The most straightforward, but not necessarily the easiest or most practical, strategy may be simply increasing the dose and intensity of exercise, although this should probably not be done too soon after stroke. Although constraint-induced motor therapy has been demonstrated to be effective, the ideal timing and format of other general exercise strategies that might be widely implemented are yet to be determined. The strategies with the best data to date are VNS and transcranial direct current stimulation, with encouraging results on mirror therapy, virtual reality, and porcine neuropeptide. Results of functional electrical stimulation, transcranial magnetic stimulation, and robotics are mixed, and little evidence supports any type of pharmacologic intervention.

CONCLUSION

The practicing neurologist will consult and collaborate with rehabilitation professionals from the first days through at least the first several months following a stroke as their patients complete inpatient and outpatient rehabilitation. Neurologists play an important role in patient advocacy for stroke recovery, especially during acute care, in minimizing potentially detrimental medications and arranging inpatient rehabilitation facility evaluation when appropriate. Understanding the principles of and evidence behind early mobilization and exercise strategies to facilitate motor recovery and the philosophy of rehabilitation management will allow the neurologist to reinforce the importance of patient engagement and participation, ensuring the best possible recovery, level of independence, and quality of life. Many questions remain about the rehabilitation process and the best strategies to enhance motor recovery through exercise following stroke. Defining the optimal nature, characteristics, intensity, and timing of a patient's participation in task-specific and repetitious exercise to maximize motor recovery constitutes the fundamental challenge of stroke rehabilitation.

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