

Neurological Principles and Rehabilitation of Action Disorders: Rehabilitation Interventions

Neurorehabilitation and
Neural Repair
Supplement to 25(5) 335–435
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DOI: 10.1177/1545968311410942
<http://nnr.sagepub.com>


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This third chapter discusses the evidence for the rehabilitation of the most common movement disorders of the upper extremity. The authors also present a framework, building on the computation, anatomy, and physiology (CAP) model, for incorporating some of the principles discussed in the 2 previous chapters by Frey et al and Sathian et al in the practice of rehabilitation and for discussing potentially helpful interventions based on emergent neuroscience principles.

Introduction

Much of the evidence-based body of knowledge informing upper-limb rehabilitation has been generated from research with patients recovering from stroke. It is not surprising, given the number of affected individuals worldwide, that stroke would serve as the dominant model. However, many principles informing neurorehabilitation interventions can be translated from stroke into interventions for other neurological conditions when appropriate.

Whenever possible, our recommendations are based on randomized clinical trials (RCTs). Unfortunately, there have been only a handful of RCTs, most of them carried out with small sample sizes. Hence, current recommendations could be overturned by a relatively small number of robust trials (ie, with a larger sample size).¹ If evidence from RCTs is not available, we refer the reader to current evidence-based guidelines developed in different countries (Box 1). These guidelines also take into consideration interventions for which the evidence is preliminary, based on nonrandomized trials or case series. Finally, we present a framework for thinking about potentially helpful interventions based on emergent neuroscience principles, as outlined in the chapters by Frey et al and Sathian et al.

It is important to keep in mind that not all movement disorders are amenable to therapy interventions alone. Some individuals will benefit from pharmacological, surgical, or orthotic interventions to reduce impairment that limits functional ability. Persistent pain can interfere with the motivation and the ability of individuals to participate in rehabilitation and pain management should take clinical priority.

General Principles for Delivery of Therapy Interventions

Delivery of therapy interventions is multifaceted, and certain general principles should be considered in each patient:

1. The establishment of a ‘contract’ between people with neurological deficits and their therapy team.
2. Analysis of behavioral deficits in relation to known principles of brain organization.
3. Sensitive and objective measurement of motor impairment and function before/during treatment.
4. Whether the aim of intervention is to restore neurological function or to adapt to its loss, and more generally the prognosis after the intervention.
5. The amount of therapy provided over what time period (dose).
6. The therapeutic environment for motor learning.

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Box 1. Links to evidence-based clinical guidelines

- National clinical guidelines for stroke: Royal College of Physicians of London, www.rcplondon.ac.uk/resources/stroke-guidelines
- Canadian Stroke Network Guidelines: evidenced-based review of stroke rehabilitation, www.ebrs.com/resources.php
- Clinical guidelines for stroke rehabilitation and recovery: www.strokefoundation.com.au/clinical-guidelines
- Guidelines on Cognitive Rehabilitation: www.guideline.gov/browse/by-topic.aspx

Rehabilitation Contract

Neurological rehabilitation is an active participatory process involving a dynamic interaction between the person with neurological deficits and the health professional members of the team. Appreciating the amount of effort required to achieve agreed-on functional goals and establishing a framework for the interaction among everyone participating is necessary to obtain an ideal balance concerning perceived effort (both the patient's and therapist's viewpoint), maintenance of attention and motivation, and expectation of the rewards and benefits of and satisfaction with rehabilitation. Frey et al discuss at least 3 mechanisms through which reward interacts with movement. Interactions between the basal ganglia and the prefrontal cortex are important for goal selection on the basis of expected or predicted reward, to reinforce movements based on expected reward, and for switching to novel actions. Although there is no direct evidence that establishing a rehabilitation contract taps into any of these mechanisms, it is important to realize that setting the right expectations will ultimately affect the perceived success or failures of therapy, and this will in turn lead to stronger or weaker learning of compensatory movement or strategies.

Underpinning agreement of goals are 2 key areas of understanding that (1) the therapist is aware of what is important for the patient and (2) the patient appreciates the mechanisms of recovery, the need to maintain ability, and the need to prevent secondary complications. Active communication is therefore a prerequisite for active participation. It is important to use enhanced communication strategies, including the following: chunking information into small bits; using diagrams, facial expressions, or gestures; and frequent checking for understanding of key messages conveyed by all conversation partners.

The setting of goals must be consistent with the likely outcome expected for that patient. Sathian et al review a number of variables that allow some "average" prediction of motor outcome. Although average estimates may not apply to specific individuals, it is important for the therapist to set realistic

expectations. For instance, in a patient with no voluntary movements of the hand at 1 month poststroke, it is not realistic to set up full recovery of hand function as a goal (please refer to detailed discussions of this point in Sathian et al). Great care is required to ensure that the provision of information does not diminish motivation for participation in rehabilitation. Indeed, preliminary evidence indicates that signing a rehabilitation contract is associated with improved functional recovery and, simultaneously, increased cortical grey matter.

Analysis of Deficits and Pathophysiology

Based on the CAP principles established in Frey et al and the diagnostic examinations described in Sathian et al, it is important that the clinician (rehabilitation physician or therapist) develops an understanding of the neurological mechanisms of the patient's observed impairment. Does the motor deficit reflect primarily an output, planning, or sensory feedback problem? Is there any problem with ataxia? Do the deficits primarily involve skilled or gross movements?

Ideally a behavioral analysis should be complemented by anatomical information about lesion location and size. For example, the presence of a small lesion in the subcortical white matter that damages only some of the corticospinal tract may be expected to be associated with greater recovery than a lesion in the brainstem that completely severs descending fibers. Similarly, a small lesion in the motor cortex may be expected to produce some clumsiness early on but good recovery overall, given compensation from other premotor regions. Bilateral lesions in the cerebellum are expected to cause more long-lasting ataxia than unilateral lesions. Although formal neuroscience-based principles for assessment and planning of therapy are not yet established, it is important that therapists begin to incorporate some of the principles discussed above as they plan their therapy. In the near future, it is expected that as neural analyses of functional recovery improve, more specific parameters based on imaging or other methods will become more clinically applicable.

Sensitive and Objective Measurements of Motor Impairment and Function

The chapter by Sathian et al provides a number of scales describing the motor status of a patient before and during rehabilitation. The key point we are adding is that measurements should be objective and free of bias, ideally performed at the beginning of the intervention and at the end by therapists who are not primarily treating the patient.

Restorative Versus Adaptive Emphasis, and Outcome

Restorative interventions are thought to improve impairment of function and to work directly on modifying the underlying neural mechanisms. Adaptive interventions provide an

alternative strategy to perform the same task. For instance, whereas task-oriented repetitive training is a restorative intervention, training to use an assistive device, for example, a tool to grasp, may be considered adaptive.

An important consideration in deciding what rehabilitation to use is the likely outcome of a patient with a neurological injury. Clinical assessment and outcome analysis as described in the chapter by Sathian et al are necessary to decide if the planned intervention should be restorative or adaptive. From a neural perspective, the potential for reorganization is maximal early on after injury; hence, as a general principle, restorative methods should be offered to acute patients. Motor function improves rapidly in the first 6 to 8 weeks poststroke and reaches a plateau around 3 months. At the chronic stage, a key element for deciding the approach to be taken is to consider prognostic factors on recovery of function. Although these factors are average, that is, apply to a group of patients as a whole, and cannot be precisely applied to individual patients, they do provide a framework to think about what is feasible in a specific patient at a specific stage. On the other hand, there is growing evidence that even at the chronic stage, restorative interventions can be beneficial. For instance, constraint-induced movement therapy (CIMT) has been shown to work in selected groups of chronic stroke patients.

A final point to judge the feasibility of restorative interventions is the presence of any voluntary motor output irrespective of its normalcy. Traditional theories (eg, neurodevelopmental theories) emphasize the quality of movement as a prerequisite before pushing more active or intense restorative training. However, work in animals indicates that even small lesions in the motor cortex compromise the normality of movement dynamics and that any motor “recovery” should be considered actually a “reorganization” of function. Hence, modern therapy strategies emphasize that any voluntary movement, even if highly abnormal in its dynamic, should be reinforced toward improving function.

A possible strategy at the chronic stage is to attempt a restorative intervention if there are elements in the clinical examination suggesting promise. For instance, the presence of wrist extension or voluntary finger movements in 1 patient at 6 months may be used to motivate a restorative intervention for the hand. After a few weeks of intense therapy, if no improvement is detected, then, one may consider switching to more adaptive or conservative therapy, for example, range of motion, stretching, and so on, for prevention of complications.

Dose

Amount of therapy (dose) is of primary importance for outcome. Dose can be thought of in terms of intensity (number of repetitions or time per session), frequency (eg, 5 sessions a week), and duration (eg, for 6 weeks). A Cochrane review reported that in a large meta-analysis of repetitive task training for the upper or lower extremity, the amount of therapy in number of hours was positively related to effect size.¹ For

both the upper extremity and lower extremity, it was necessary to train for more than 20 hours to have a significant change in function. It is likely that higher doses may be more effective. In general, one explanation for why it is often difficult to demonstrate the benefit of rehabilitative interventions may very well be because they are routinely delivered at sub-optimal doses.

Experimental studies with animal models suggest that 300 to 400 repetitions of a task are required to learn a motor skill and to change the patterns of brain activity. This intensity is not currently achieved in clinical practice. A recent multicenter observational study in North America showed that fewer than 30 repetitions per session are currently achieved in rehabilitation practices.² Indeed, the mean number of repetitions of an active exercise and functional activity during rehabilitation sessions is low both after stroke and after traumatic brain injury and is probably dependent on the experience of the therapists.³ However, the findings of an early phase trial indicate that it is possible to achieve a mean of 322 repetitions of task-oriented training for the upper extremity in a 60-minute session and that delivery of high-repetition therapy was sustained 3 times a week over a 6-week period.⁴ An early concern regarding high-dose therapy was the observation that high levels of physical activity in rats, early poststroke, were associated with a poorer functional outcome. However, a recent clinical trial did not find a relationship between lesion volume and high-dose-activity rehabilitation.⁵

Therapeutic Environment for Motor Learning

People with neurological deficits need to learn to move again in the most energy-efficient way possible within the confines of the damage sustained. The therapist is therefore a mediator in each individual’s motor learning process. Motor learning is defined here as follows: a change in the capability of a person to perform a skill as a result of practice or experience.

Although an extensive discussion of learning is outside the scope of this chapter, some general principles can be quickly reviewed. All models of motor learning include the need for the detection of errors and production of appropriate corrective adjustments in different environmental contexts. For instance, during a reaching task, one needs to vary the features of the object to be reached (size, shape, etc), which determine the shaping of the hand and sensory feedback; the position of the object, which determines the trajectory of the movement; and the possibility to see the arm/hand before/during movement, which affects the estimation of initial state and forward models (please refer to Figure 1 in Frey et al and Figure 1 in Sathian et al).

Errorless performance leads to slower improvement than performance with a small number of errors. At the same time, an excessive number of errors leads to frustration and potentially negative feedback, which impairs optimal learning. A rule of thumb is to have patients work at 80% to 90% accuracy of their maximal capacity. Part of the role of a therapist is to provide extrinsic feedback to enhance motor learning.

A final important aspect is assessment of motor learning capacity, such as capacity for sustained attention, communication ability, and problem-solving ability. In the future, therapists might also need to consider that damage to different brain areas may affect motor learning differentially. For instance, patients with cerebellar lesions may not benefit as much from performance feedback, given their inability to learn from their errors. In this case, a more implicit strategy may be more beneficial.

Content of Rehabilitation Interventions: Specific Techniques

At present, techniques (components of interventions) used to treat different patients vary considerably across different geographical locations. This range of techniques provided in current clinical practice have, historically, been described according to different conceptual approaches. There is, however, an urgent need to validate the efficacy of this wide range of techniques and develop treatment algorithms that stack interventions and component techniques based on the level of evidence. This is critical to make the practice of rehabilitation more evidence based and less subjective.

Unfortunately, current recommendations in rehabilitation are based on relatively weak evidence that could be easily overturned by a few well-done RCTs. Each technique has been tested only by a small number of trials—typically, only 3 per method; furthermore, these trials have been underpowered, with an average of only 70 patients per trial; finally, the methodology used so far has not been optimal in terms of making the trials more objective and less prone to statistical biases. Nonetheless, there is a strong theoretical framework and several solid findings that can be used to select the most appropriate intervention. A final caveat that should be considered when reading the following section is that there is much more evidence for improving arm function than hand function. In fact, interventions to improve hand coordination and dexterity have yielded very disappointing results overall.

Specific Techniques to Reduce Paresis

The paretic upper limb is typically weak, slow, and lacking in coordination and dexterity. Spasticity may be a feature. These symptoms can appear alone or in combination. Paresis involves difficulty with or inability to modulate the production of appropriate force in the right muscles at the right time to produce a movement or perform a functional task deftly, accurately, and in an energy-efficient manner. Paresis that follows cerebral injury reflects difficulty with motor outflow either from damage to the cortical neurons or damage to the white matter fibers projecting to the spinal cord.

Based on principles developed in the first 2 chapters by Frey et al and Sathian et al, 3 principles for treatment can be defined:

1. priming techniques to increase the excitability of the stroke-affected motor system and promote plastic reorganization in response to subsequent practice of physical activity;
2. augmenting techniques applied during physical practice to enhance their effects by boosting voluntary activation of paretic muscles (in the following section, we will describe some of these interventions emphasizing those methods that have received support in RCTs); and
3. practice of task-specific exercises.

Box 2 provides a vignette to illustrate the application of some of these techniques.

Priming Techniques. Priming interventions may prepare the sensorimotor system for subsequent motor practice, thereby enhancing its effects. Brief details are given here, with a fuller version provided in Box 3.

Motor and visual imagery. These techniques can be used to internally generate somatosensory and visual input to the motor system. There is strong evidence from neuroimaging studies that mental practice and imagery can activate regions in the motor system. These signals can be conceptualized as motor plans without execution. Repetitive generation of motor plans may promote physiological patterns of activation in motor cortical circuitries that are either directly damaged or functionally impaired because of impaired outflow after damage of the corticospinal tract, abnormal forward models, or decreased activation by sensory feedback because of lack of movement. Four RCTs have shown that the addition of mental practice to physical practice can have a beneficial effect on motor performance.⁶ In one of these studies, chronic stroke patients (>12 months) were randomized to 2 groups: (1) mental + physical practice, in which twice a week for 6 weeks they participated in a 30-minute physical therapy session centered on activities of daily living (ADL) followed by a 30-minute mental practice session in which they mentally rehearsed the exercises just performed; (2) relaxation + physical practice, in which the therapy sessions were followed by a 30-minute session of mental relaxation. At 1 week postintervention, motor impairment and functional scores for the upper extremity were significantly improved in the mental practice group as compared with the relaxation group.⁷ Although the effect size is relatively robust, only a small number of patients have been tested so far (about 70 till March 2010). The duration of the intervention effect is also unknown because most postintervention measurements were obtained shortly after the end of the trial (typically 1 week).

Tactile stimulation, soft tissue mobilization, and passive movements. These methods provide sensory input that engages the patient's attention and orients the individual to the paretic limb. Passive movement has similar effects while also providing sensory feedback to the motor system.

Box 2. Vignette illustrating the use of emergent neuroscience principles to inform choice of interventions for paresis

Mrs X is a 70-year-old woman with a stroke and a paresis of the right hand (dominant) resulting from an infarct in the territory of the middle cerebral artery in the left hemisphere. Neuroimaging indicates that the infarct is subcortical in the corona radiata.

At 3 days after stroke, Mrs X is alert and has no evidence of either aphasia or visuospatial neglect, and sensorimotor function of her left upper limb is essentially normal. The right upper limb is paretic with the following characteristics: mild sensory deficit (both tactile and proprioception) and grade 2 voluntary muscle activity (able to produce muscle contraction but not against gravity) around the shoulder, elbow, and wrist. However, she is unable to produce any fractionated movement of her fingers.

Functionally, she is able to reach for a key by sliding her upper limb across a table but is unable to grasp it and use it to unlock a door. This impairment pattern is consistent with the location of the lesion.

Initially, the primary focus of therapy is restorative—that is, to facilitate biological recovery and improve upper-limb functional ability. Mrs X is able to produce some voluntary muscle activity for reaching but is unable to grasp objects. Key interventions provided are the following: therapist-assisted repetitive practice of reaching, electromyographic biofeedback of muscle activation (visual display of wrist extension activity) during reaching, tactile stimulation and mobilization of soft tissues of the hand, passive movements of the paretic hand while encouraging Mrs X to join in the movement, motor imagery training of both reaching and grasping, and functional electrical stimulation of grasp/release as the ability to voluntarily activate paretic muscle improves. As she gains the ability to contract paretic muscles in an appropriate temporal-spatial pattern, resistive training is added to practice of reaching. Throughout this intensive treatment period, which may last for approximately 6 weeks, Mrs X is given the rationale for interventions and encouraged to pursue self-directed activities.

At 3 months after stroke, Mrs X has sufficient fractionation of fingers to reach to a shelf at eye level and pick up the key, albeit abnormally, but is unable to insert it into the lock. A rehabilitation service may or may not be available as provision varies across the globe. On the assumption that rehabilitation is available, testing indicates that improvement in the paretic upper limb has slowed down and is more evident in hand than in arm function. The primary focus of therapy therefore changes from facilitating recovery (restorative) to enabling Mrs X to

(continued)

Box 2. (continued)

compensate for hand paresis. Strategies could include signing documents with her left hand (nondominant) and providing adaptations to a key to reduce grasp requirements. Such strategies provide the benefits of increasing independence but could lead to learned nonuse of the paretic upper limb. These strategies therefore need to be used judiciously.

Mrs X is therefore introduced to constraint-induced movement therapy to ensure that she continues to use her paretic upper limb for functional activity as part of a planned program. Again, as in the earlier rehabilitation phase, Mrs X is given information about the rationale for intervention and is encouraged to undertake self-directed motor activities. It should be appreciated that in some health care settings very few stroke survivors receive any therapy after the initial rehabilitation period.

Box 3. Priming techniques to reduce paresis

Tactile stimulation and soft tissue mobilization provide sensory input that engages the patient's attention to their paretic limb. Passive movement has similar effects while also providing a sensory template for desired movements. There is preliminary evidence for this module of conventional therapy.

Motor imagery and visual imagery can be used to internally generate somatosensory and visual input to the motor system. During mental practice, the patient rehearses the planning and preparation components of activities of daily living, particularly when actual practice may be limited by impairment or fatigue. Imagining the somatosensory consequences of movement (motor imagery) has been shown to activate the motor cortex and may serve to reinforce the sensorimotor templates of desired movements. There is some evidence that mental practice can improve upper-limb function, but further studies are needed to determine the optimal dose and characterize the patients most likely to benefit.

Action observation and mirror therapy use visual input for priming. The patient observes specific movements or tasks performed by the therapist or by their nonparetic limb reflected in a mirror placed at the body's midline. By placing the paretic limb behind the mirror, the reflected movements of the nonparetic limb appear to be performed by the paretic limb. Both these techniques are thought to activate the motor system and prepare it to perform the observed actions with the paretic limb. Mirror therapy can also be

(continued)

Box 3. (continued)

used as an augmenting technique during practice. Studies of healthy adults suggest benefit, and there is preliminary evidence that they improve upper-limb function following stroke.

Some priming techniques specifically aim to alter neurotransmission, balance motor cortex excitability between the 2 hemispheres, and enhance neural plasticity. This balance can be achieved with stable movement patterns, such as active–passive bilateral therapy (APBT). During APBT, the patient produces rhythmic flexion–extension of a nonparetic joint in a mechanical device that produces passive mirror-symmetric flexion–extension of the corresponding paretic joint. Preliminary studies of wrist APBT performed prior to motor practice found lasting reductions in impairment and balancing of motor cortex excitability. These effects are most likely a result of the mirror-symmetric movement pattern and the number of passive movement repetitions being much greater than could be achieved actively in each session. Further studies are required to determine the optimal dose and characterize those most likely to benefit.

Magnetic stimulation techniques can be used to alter motor cortex excitability prior to practice. Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive technique that delivers brief magnetic stimuli over the scalp, activating the underlying cortex, at a low frequency (1 Hz) for up to 15 minutes or at higher frequencies (10–50 Hz) for as little as 3 s. rTMS can either increase or decrease the excitability of the underlying cortex, depending on the frequency and pattern of stimuli. It has been used to increase ipsilesional motor cortex excitability and decrease contralesional motor cortex excitability in stroke patients. These effects appear to improve functioning of the paretic upper limb, particularly when delivered prior to motor practice. It should be noted that rTMS is more suitable for patients with a largely intact motor cortex and is contraindicated in patients with cardiac pacemakers or a history of seizures.

Transcranial direct current stimulation (TDCS) is another noninvasive technique for stimulating the cortex of the brain. It involves passing a low current (1 or 2 mA) between 2 electrodes on the scalp for 10 to 30 minutes. The underlying neurons are polarized and become more or less excitable, depending on the polarity of the overlying electrode. As with rTMS, TDCS has been used to increase ipsilesional excitability or decrease contralesional excitability in stroke patients. There is preliminary evidence that these effects are associated with improved function of the paretic upper limb. TDCS can be applied

(continued)

Box 3. (continued)

before and during motor practice, making it both a priming and an augmenting technique. Similar benefits may be produced by stimulating the cortex with implanted electrodes, and this technique is being development. As with rTMS, these techniques are more suitable for patients with a largely intact motor cortex.

Pharmacological agents can be used to alter neurotransmission and the excitability of the motor cortex. It is possible that drugs such as amphetamines and dopamine agonists improve motor function when administered prior to therapy to both prime and augment the effects of motor practice. Selective serotonin reuptake inhibitors may have beneficial effects on the motor system, distinct from their antidepressant actions. Further clinical trials are needed to draw definite conclusions, and it should be noted that unlike other priming and augmenting techniques, drug actions are not hemisphere specific.

Action observation, mirror therapy. These techniques use visual input for priming. The patient observes specific movements or tasks performed by the therapist or by their nonparetic limb reflected in a mirror placed at the body's midline. In the first chapter in this series, we discussed frontoparietal circuitries that respond not only during one's own movement but also during the observation of others' movements. Observation may promote activation of these circuitries. A recent RCT of mirror therapy demonstrated improvement in motor function.⁸

Repetitive transcranial magnetic stimulation (rTMS). rTMS noninvasively delivers brief magnetic stimuli over the scalp, activating the underlying cortex, at a low frequency (1 Hz) for up to 15 minutes or at higher frequencies (10–50 Hz) for as little as 3 s. rTMS can either increase or decrease the excitability of the underlying cortex depending on the frequency and pattern of stimuli. One possible future application of rTMS is to prime the excitability of the motor cortex prior to rehabilitation.

Transcranial direct current stimulation (TDCS). TDCS is another noninvasive technique for stimulating the cortex of the brain. TDCS involves passing a low current (1 or 2 mA) between 2 electrodes on the scalp for 10 to 30 minutes. The underlying neurons are polarized and become more or less excitable, depending on the polarity of the overlying electrode.

Pharmacological agents. Drugs like methylphenidate or dextroamphetamine have been tried alone or in combination with motor rehabilitation to enhance recovery.

Augmenting Techniques. Augmenting techniques are thought to enhance aspects of sensorimotor function during practice. Brief details are given here with a fuller version provided in Box 4.

Box 4. Augmenting techniques to reduce paresis

Therapist- or robot-assisted movement of the paretic upper limb provides the motor system with the sensory feedback it would receive if it were able to move normally. This sensory feedback is thought to facilitate the motor system and provide a template of desired movement patterns. Robotic devices can also be used to guide voluntary movements along optimal trajectories to reinforce desired movements. There is some evidence that robotic devices can reduce shoulder and elbow impairment, and their impact on wrist and hand function may increase with further developments in their design.

Biofeedback provides patients with visual and/or auditory feedback of the timing and strength of their muscle activation. This approach is directed at helping individuals to gain greater conscious control over components of the practiced movement, although at present, there is no clear evidence of its efficacy.

Functional electrical stimulation (FES) and transcutaneous electrical nerve stimulation (TENS) can be used to activate muscles and generate sensory input. In particular, FES can be used to enhance the voluntary activation of elbow, wrist, and finger extensors during reach-to-grasp and other functional tasks. There is some evidence that these techniques can reduce impairment, but further research is required to confirm this and establish the optimal dose.

Some augmenting techniques specifically aim to alter the balance of excitability between the 2 hemispheres during practice. Generally, the aim is to increase ipsilesional excitability and/or decrease contralesional excitability. One example is TDCS, which can be used for both priming and augmenting and which has been described earlier.

Bilateral training involves performing activities such as reaching and grasping with both arms simultaneously. This approach may improve task performance with the paretic upper limb because of the facilitation of paretic muscle representations in the motor system by their healthy counterparts on the opposite side. Although the evidence for bilateral training to date is mixed, those patients with greater impairment, who are more likely to recruit contralesional motor cortex activity in the brain during paretic limb movement, may benefit the most.

Constraint-induced movement therapy (CIMT) involves therapist-directed practice and self-directed motor activity with the paretic arm while the opposite arm is restrained. CIMT aims to rebalance motor cortex activity by increasing the activity of the paretic arm with massed practice while restricting the activity of the opposite limb. There is strong evidence that this approach is beneficial, particularly for patients at least 3 months after stroke with at least 10° of active wrist and finger extension. Further study is required to determine the optimal dose in terms of contact hours and their distribution.

Constraint-induced movement therapy. CIMT is the only intervention that has been validated by many different trials (21 with more than 500 patients enrolled) and in a prospective multicenter RCT. It should therefore be considered as the first choice for patients who qualify.⁶ CIMT therapy is based on the notion that brain injury leads not only to structural damage but also to physiological impairment of motor pathways/regions. Specifically, injury leads to depression of neural excitability near the lesion, which, coupled with negative feedback from unsuccessful attempts, leads to further decrement of excitability and, secondarily, a learned nonuse of the paretic arm. There is also evidence of impaired interhemispheric interaction with increased excitability in the contralateral (normal) motor cortex that can exacerbate the learned nonuse. It is indeed a common clinical observation that patients after a stroke tend to use their paretic arm less and less over time. The intervention is based on constraining movements in the normal arm, for example, by asking patients to wear a mitten during waking hours while intensely training the weak arm. There are other important elements to CIMT, such as the execution of task-specific exercises (eg, reaching, turning, opening, etc), the high dose (4-6 h/d), and “shaping.” This involves a complex set of interactions in which the therapist both sets the difficulty of the exercises to a level that the patient can successfully perform most of the time while at the same time providing feedback and encouragement on the errors. As discussed earlier, errors are necessary to learn as they provide a training signal for change. It is currently unknown which combination of factors is most important. The value of CIMT has been demonstrated in chronic patients, whereas in subacute patients (1-3 weeks poststroke), a recent study did not show a differential effect above standard therapy. Another strong limitation is that only patients who have 10° to 20° of wrist flexion can benefit from this therapy; unfortunately, this group represents only a minority of all stroke patients (about 20%).

Electromechanical or robotic-assisted therapy. A number of different devices have been designed for aiding the movement of the paretic upper extremity during tasks such as reaching for a visual target. These systems provide the motor system with the sensory feedback it would receive if it were able to move normally, which, in turn, may increase excitability in motor pathways. Vision of the arm in movement may also activate circuits related to action observation. The interest in robotic-assisted movements is also instrumental to the notion of providing high doses of therapy in a relatively inexpensive way. Although early generation robots provided assistance with a fixed torque, that is, the same torque irrespective of the patients’ voluntary contraction, more recent models can “feel” the patient’s movement and adjust the degree of assistance. In 1 meta-analysis (10 trials with about 200 patients), a moderate overall size effect was obtained, but the small sample size of each study prevented stronger conclusions.⁶ A recent meta-analysis compared numerous RCTs of robotic-assisted

movement therapy (11 studies with more than 300 patients and fewer than 50 patients per trial) with other methods (standard physical therapy, free reaching, electrical stimulation-triggered movement, and resistive robotic therapy) while matching the dose of the intervention.⁹ A typical training schedule consists of a 30- to 90-minute session 5 days/week for 3 to 12 weeks (ie, about 15-60 hours of training). Whereas weak effects were demonstrated on ADL and only for patients less than 3 months poststroke, robust effects were found on motor strength and function. This intervention may therefore be an important adjuvant to standard physical therapy, but again, dose effects may be of utmost importance.

Electromyographic (EMG) biofeedback. This set of methods provides patients with visual and/or auditory feedback of the timing and strength of their muscle activation recorded via a surface EMG electrode. Although the putative neural mechanisms behind this method are unknown, recent evidence indicates that patterns of cortical activity can be modulated with biofeedback. This method has been tested in a small number of RCTs (4 trials, <150 patients) and has been shown to have a small to moderate effect overall.⁶ In a few studies, robust effects on range of motion and strength were obtained.¹⁰

Functional electrical stimulation (FES) and transcutaneous electrical nerve stimulation (TENS). FES and TENS can be used to activate muscles and generate sensory input. This technique has been studied in a fair number of RCTs (13 trials on >250 patients), and its effects on movement are small to moderate overall.⁶ From a physiological standpoint, it appears that the ability to facilitate voluntary movements generated by the patient through electrical stimulation (FES) would be much more desirable than electrically inducing movements. Natural movements are produced by delicate and complex patterns of muscle activity that are not reproduced by the nonspecific and massive activation produced by TENS. In the near future, it will be possible to interface brain signals recorded, for instance, through EEG during movement planning, imagery, or execution and use those signals to drive peripheral devices or for enhancing movements of the affected arm. Closing the loop with the brain will allow a more specific and timely form of functional stimulation.

Bilateral training. Bilateral training involves performing activities such as reaching and grasping with both arms simultaneously. It is based on the notion of disrupted interhemispheric interactions (see Box 3 in Sathian et al, this issue). This technique has been tested in a small number of trials (2 RCTs and 122 patients), and its effectiveness is unknown.

Task-Specific Practice. In addition to specific methods, a more general set of principles that are thought to be essential in rehabilitation includes the notion of task-specific practice. Practice is the core of therapy. The repeated performance of a specific movement or task can produce meaningful improvements in function. Practice improves performance by providing the central nervous system with repeated opportunities to estimate the body's state and integrate this with a movement goal; produce

appropriately sequenced, timed, and scaled motor commands; and adjust motor output on the basis of sensory feedback.

The strongest scientific rationale at present is for task-specific practice based on principles of experience-dependent motor cortex plasticity. Task-specific practice can include shaping of the patient's performance by identifying key components of the task (such as movement speed or distance) and providing positive verbal feedback with each small improvement in these components while progressively increasing the task demands. Task-specific practice elements are present in most of the techniques described above and intersect strongly with the issue of dose discussed above. A recent meta-analysis compared repetitive task training with either no intervention or other training (attention and strength; 13 RCTs and >600 patients) with a variable amount of practice (from <10 hours to >40 hours) and for periods of 2 to 6 weeks. Overall, a trend of a positive effect for arm function was found, but there was no effect for hand function. However, when the efficacy was compared as a function of dose, it was found that the effect was nearly double in patients with more than 20 hours of practice as compared with patients with 0 to 20 hours of practice.¹¹

Specific Techniques to Reduce Apraxia and Motor Neglect

Apraxia. Apraxia reflects a problem with high-level motor planning and the retrieval of stored knowledge for the generation of actions. Historically, it was believed that limb apraxia had little if any impact on everyday activity. Now, it is widely held that limb apraxia is an important determinant of dependence in activities of daily living after stroke. For example, limb apraxia (ideational and ideomotor) may increase clumsiness in object manipulation and be detrimental to daily life activities. Therefore, during the initial assessment of patients, the presence and severity of limb apraxia should be determined.

Standardized testing batteries derived from cognitive models of limb apraxia are currently available. However, for clinical practice, it is important for the clinician to understand if the patient suffers from apraxia in addition to motor deficits per se. Observing whether a patient uses tools correctly or pantomimes their use correctly during ADL training is sufficient to screen for the presence/absence of ideomotor apraxia. Ideational apraxia can be screened by asking the patient to execute or pantomime a complex sequence of actions (eg, striking a match to light a candle or making coffee).

There is a paucity of systematic research into therapeutic techniques for treating apraxia.¹ Evaluations of the reduction in specific movement errors have been undertaken in individuals by using verbal or physical cues on how to position specific upper-limb segments during action execution. Breaking the task into different components or systematic withdrawal of facilitation cues have also been tested. All these approaches, however, have been carried out in single case

subjects, and no generalization effects or influence on daily life activities have been investigated.

Thus far, a small number of systematic treatment approaches to apraxia rehabilitation have been evaluated in groups of patients. One of these is the strategy training approach developed specifically as a compensatory technique for patients in whom apraxia negatively influences ADL. This method is based on the notion that goals and actions are composed of subgoals and that these subgoals can be accessed by a variety of inputs (verbal or pictorial; see Box 1 in Frey et al). This method focuses on the use of internal (eg, patients use language to describe the task and reinforce themselves) or external strategies (eg, use of pictures). This approach was found to be more effective than standard occupational therapy in improving ADL.¹² The beneficial effects were maintained 5 months after stroke and to some extent generalized to untrained everyday activities.

Another approach is the errorless completion method in which patients imitate the activity performed by the examiner. This aims to reduce the errors made by the patient with the rationale that errors do not help patients relearn but introduce further noise. This technique was compared with the exploration training method that is not based on direct practice but on perceptual attention to the functional significance of details and critical features of the action to be performed. Hence, in one case, the patient directly practices, whereas in the other case, the patient attentively observes. These 2 methods were applied to 2 different ADLs performed by patients with chronic limb apraxia. Although the exploration method was ineffective, the errorless completion method had a lasting facilitation effect. However, this did not generalize to untrained everyday activities.¹³

The reported findings that action observation and action execution are based on largely overlapping neural networks in the ventral parietal and frontal cortex (as described in Frey et al) have inspired the development of novel intervention techniques. The training consists of 3 progressive phases, each of which is characterized by an increasing degree of difficulty. For example, in phase 1 of gestures training, patients were shown the use of common tools and then requested to imitate the examiner. In phase 2, patients had to perform a given gesture after having seen a depiction of part of the same gesture. In phase 3, patients had to perform the gesture corresponding to the object shown in a picture. Measures were made to determine whether a given action was performed correctly. This type of treatment was found to be effective as compared with standard apraxia treatment, although it required up to 35 sessions. What is of importance is that both subjective and objective improvements in ADLs were found 2 months and 2 weeks after treatment, respectively. Box 5 provides a vignette to illustrate the application of some of these techniques.

Motor neglect. No study to date has tested rehabilitation techniques specifically designed for improving upper-limb action in motor neglect, defined as the failure to initiate limb movement on one side because of an attentional deficit rather

Box 5. Vignette illustrating the use of emergent neuroscience principles to inform the choice of interventions for apraxia

Mr Y has sustained a stroke in the left hemisphere resulting from an infarct in the middle cerebral artery. Neuroimaging indicates that the lesion extends through the frontal-parietal-temporal area. He is 52 years old and is a plumber. At 3 days after stroke, Mr Y has evidence of aphasia (mild anomia and mild comprehension impairment) and mild/moderate paresis in his right upper limb. During the day, it is noticed that he mixes up objects on his food tray and makes sequence errors (open/pour cereal) but has intact object recognition.

In terms of our target behavior, he is able to reach and grasp the key using his right hand but with a variety of abnormal grips, attempts to turn it before approaching the lock, and then makes clumsy attempts to place the key, held in various orientations, into the lock. Similar problems are observed when using the left hand. Clinical examination reveals difficulty in both action production and perception. Defective performance involves pantomime execution as well as recognition and identification of transitive and intransitive pantomimes. Gesture production in response to seeing and/or holding actual tools or the objects on which the tools act is also impaired.

Initially, the primary focus of therapy is restorative and aims to facilitate recovery of both conceptual and execution aspects of gesture production and comprehension. The key intervention provided consists of a therapist-assisted behavioral training program consisting of gesture production and gesture recognition exercises. Training of both transitive and intransitive gestures is contemplated. Increasing complexity of the training tasks is obtained by a phased reduction of facilitation cues as performance improves. The treatment period may last for approximately 4 to 5 weeks (this is influenced by different health care delivery systems). Mr Y is given the rationale for interventions and encouraged to pursue self-directed activities.

At 3 months after stroke, Mr Y shows improvement in the ability to perform gestures in response to specific verbal and also visual requests. Comprehension of conceptual and executive aspects of gestures is improved. Crucially, performance of daily living activities is also improved. Mr Y is encouraged to undertake self-directed gestural production and motor planning activities. Beyond 3 months, intermittent therapy sessions are delivered on request from Mr Y or his family if and when they notice that ADL problems reappear. In these later stages after stroke, it is recognized that rehabilitation services may or may not be available and that this varies with geographical location.

than because of an impairment to primary motor systems or learned nonuse. The lack of a gold standard test for assessing motor neglect has made it difficult to test techniques specifically designed for treating motor neglect. It is worth noting, however, that CIMT or possibly bilateral arm training could be of benefit.¹⁴

Specific Techniques to Reduce Ataxia

Ataxia is often associated with damage to the cerebellum or its connections. Ataxia caused by disruption of cerebellar input includes loss of proprioception as a result of dysfunction of spinal dorsal columns or vestibular dysfunction. In terms of the CAP model, this produces a disturbance in forward modeling of intended movements. The result is uncoordinated movements. A large variety of pharmacological treatments have been tried (eg, isoniazid, pyridoxine, and baclofen) but have not shown consistent results. Preliminary research suggests that CIMT may improve reaching kinematics and real-world limb use among individuals who have developed poststroke ataxia.¹⁵

Tremor and other involuntary hyperkinetic limb motor disorders after brain injury are associated both with cerebellar and basal ganglia dysfunction. Drugs are often used for management (eg, propranolol, primidone, and sertraline). More recently, tremor has been successfully treated with deep-brain stimulation of sites in the basal ganglia and thalamus. Preliminary research has suggested that adopting rhythmic limb movements during physical therapy can reduce involuntary limb movements after stroke and thus may allow improved treatment participation.¹⁶

Because ataxia and tremor interfere with normal limb use, teaching patients strategies to cope with these deficits can be useful.

Specific Techniques to Maintain Integrity of Effectors

An important part of neurorehabilitation is the use of techniques that are designed to maintain or protect the integrity of upper-limb joints and muscles during periods of suboptimal movement performance. For example, in the presence of paralyzed muscle early after stroke, there is a risk of shoulder pain and/or glenohumeral dislocation. Another example is the development of muscle hypertonicity and/or contractures in the presence of permanent CNS damage. These techniques include those described below.

Exercise and stretching are used in the first instance to reduce spasticity. For people with constant focal spasticity in the absence of contracture, botulinum toxin is used intramuscularly. For those people experiencing generalized spasticity, antispastic drugs, for example, baclofen, can be given. All drugs should be administered within an expert neurorehabilitation setting and accompanied by specific techniques (outlined earlier in this chapter) designed to gain motor

function as spasticity subsides. If contractures develop or are likely to develop, then a program of stretching and splinting should be considered.

To prevent and treat shoulder pain and glenohumeral subluxation, considerable attention is provided to positioning of the upper limb 24 hours a day, which is accompanied by expert moving and handling techniques. Particular positioning and moving and handling techniques are specified for each individual and used by each member of the neurorehabilitation team, including the patient and their informal caregivers. There is, therefore, an emphasis on education personalized for each individual that centers on the normal anatomy of the shoulder complex, the disruption caused by neurological damage, and the specific techniques to minimize disruption and prevent further damage. Specific supports, for example, foam wedges, may be used for the upper limb. Simple analgesia may be given regularly. For individuals with troublesome pain, the neurorehabilitation team will consider use of shoulder strapping, high-intensity transcutaneous nerve stimulation, or FES.

Future Clinical Directions

Recent advances in the scientific rationale and evidence base for neurological rehabilitation have, over the past 10 years, changed the clinical emphasis from that of treatment approaches to specific techniques for particular aspects of upper-limb movement dysfunction. This change has accompanied an exponential increase in research over the last 20 years.¹⁷

Most interventions that have been proposed and tested have typically concentrated on improving 1 specific mechanism (learned nonuse, decreased excitability, disrupted interhemispheric interactions, etc). However, the principles discussed in the CAP show that motor deficits can arise from different computational problems and that a single lesion is likely to cause multiple problems both through direct structural damage and impaired function of distant and connected regions. In an ideal future, a patient would receive in-depth assessments that quantify his or her motor deficits through careful behavioral testing; neuroimaging measures of structure, function, and connectivity; and computational modeling. This assessment would allow the characterization of the patient's deficit with a small number of different parameters that ideally would be sensitive to changes over time and final outcome. For argument's sake let us assume that 3 parameters (intactness of output, normalcy of forward models, and sensory feedback) describe the great majority of behavioral variance of a normal movement. And, let us also assume that these parameters provide a good description of an individual's hemiparesis. For example, in the case of a lesion interrupting the corticospinal tracts, output parameters will be prominently affected, whereas forward models and sensory feedback would be less affected. With time, all 3 parameters may worsen because an attempt by the cortex to overcome the bottleneck caused by the lesion will generate more errors in the forward

model that will accumulate over time. Accordingly, therapies should be first aimed at improving the motor outflow through, for example, excitatory stimulation of the damaged motor cortex. At the same time, however, other methods can be applied to improve the other parameters. A decrement in sensory feedback could be helped by robotic therapy, whereas a problem in the forward model could be lessened by motor imagery exercises. Critically, which cocktail or dosing of treatments to apply will depend on a deeper understanding of the system, its abnormal output after lesions, and its response to therapy. It is very likely that targeted interventions will be more likely to produce positive results than single-mode treatments. It will be important to develop prognostic models also to avoid the “one model fits all” approach currently used in rehabilitation. As resources in health care are limited, identifying patients with a good chance for recovery is as important as identifying patients with a poor chance of recovery in whom compensatory strategies or orthotic devices should be tried earlier. Moreover, improvements in technology that are already being tried will profoundly modify the assisting devices that we will be able to provide. Whether this vision will be realized in 10 years or never will be a matter of persistence, money, and the intellectual discipline to continue pursuing a science of rehabilitation.

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