Motor learning: its relevance to stroke recovery and neurorehabilitation

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Purpose of review

Much of neurorehabilitation rests on the assumption that patients can improve with practice. This review will focus on arm movements and address the following questions: (i) What is motor learning? (ii) Do patients with hemiparesis have a learning deficit? (iii) Is recovery after injury a form of motor learning? (iv) Are approaches based on motor learning principles useful for rehabilitation?

Recent findings

Motor learning can be broken into kinematic and dynamic components. Studies in healthy subjects suggest that retention of motor learning is best accomplished with variable training schedules. Animal models and functional imaging in humans show that the mature brain can undergo plastic changes during both learning and recovery. Quantitative motor control approaches allow differentiation between compensation and true recovery, although both improve with practice. Several promising new rehabilitation approaches are based on theories of motor learning. These include impairment oriented-training (IOT), constraint-induced movement therapy (CIMT), electromyogram (EMG)-triggered neuromuscular stimulation, robotic interactive therapy and virtual reality (VR).

Summary

Motor learning mechanisms are operative during spontaneous stroke recovery and interact with rehabilitative training. For optimal results, rehabilitation techniques should be geared towards patients' specific motor deficits and possibly combined, for example, CIMT with VR. Two critical questions that should always be asked of a rehabilitation technique are whether gains persist for a significant period after training and whether they generalize to untrained tasks.

Keywords

hemiparesis, motor control, motor learning, reaching, rehabilitation, stroke recovery

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Abbreviations

ADL activities of daily living
CIMT constraint-induced movement therapy
EMG electromyogram
VR virtual reality

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Introduction

'Rehabilitation, for patients, is fundamentally a process of relearning how to move to carry out their needs successfully' [1]. This statement succinctly points out the fact that rehabilitation is predicated on the assumption that practice or training leads to improvement of skills after hemiparesis. Despite this underlying assumption, research in motor control and motor learning has only recently begun to make an impact on the practice of rehabilitation. Instead, stroke rehabilitation has focused either on passive facilitation of isolated movements or teaching patients to function independently using movements alternative to the ones they used before their stroke. In addition, inordinate emphasis has been placed on therapy for spasticity despite substantial evidence indicating that it does not make a significant contribution to movement dysfunction [2].

Motor control and motor learning in healthy subjects

Motor learning does not need to be rigidly defined in order to be effectively studied. Instead it is better thought of as a fuzzy category [3••] that includes skill acquisition, motor adaptation, such as prism adaptation, and decision making, that is, the ability to select the correct movement in the proper context. A motor skill is the ability to plan and execute a movement goal. The computational steps required to go from goal to action for reaching movements have been extensively studied over the last 20 years (see the monograph by Shadmehr and Wise [3••]) but the knowledge of motor control gained has only recently begun to be applied to the characterization and treatment of the motor deficit after hemiparesis.

Motor control scientists make an important distinction between the geometry and speed of a movement (kinematics) and the forces needed to generate the movement (dynamics). This distinction can be better understood by imagining tracing a circle in the air with your hand or with your foot. The circle may have the same radius and be traced at the same speed with the hand and the foot, but completely different muscles and forces are needed to generate the circle in the two cases. Similarly, reaching trajectories involving more than one joint consistently have near-invariant kinematic characteristics: straight paths and bell-shaped velocity profiles [4], which suggest reaching trajectories are planned in advance without initial need to take account of limb dynamics. In the execution phase, motor commands take the complex viscoelastic and inertial properties of multi-jointed limbs into account so that the appropriate force is applied to generate the desired motion. Thus motor control is modular [5], even a simple reaching movement is made up of separate operations, each of which may or may not be affected by a lesion. Within this motor control framework, skill acquisition can be understood as practice-dependent reduction of kinematic and dynamic performance errors detected through visual and proprioceptive sensory channels, respectively [6].

An experimental paradigm that is widely used to study motor learning involves having subjects hold the handle of a robotic arm and make planar reaching movements in a horizontal plane to visual targets displayed on a screen [7]. Motors driving the robot arm can be programmed to generate specific force-fields that act upon the moving arm. One type of force-field, called a viscous curl field, generates forces perpendicular to the direction and proportional to the velocity of hand movement. Before the motors are switched on, subjects are able to hold the handle and make reaching movements with smooth and straight trajectories. When first exposed to the viscous curl field, subjects make skewed trajectories, but with practice are able to adapt to the force-field and again make smooth and nearly straight movements. When subjects are in this adapted state and the force-field is turned off, 'after-effects' occur, with trajectories now skewed in the direction opposite to that seen during initial adaptation. The presence of after-effects is strong evidence that the central nervous system can alter motor commands to the arm to predict the effects of the force-field and form a new mapping between limb state and muscle forces (internal model). Experiments indicate that internal models learned for one type of movement can generalize to other movements [8]. The importance of the concept of internal model to rehabilitation is that the model can be updated as the state of the limb changes. Thus rehabilitation needs to emphasize techniques that promote formation of appropriate internal models and not just repetition of movements. As we shall see below, variations on this robot paradigm have been used to investigate motor learning in patients with hemiparesis and to build robotic assistive devices for rehabilitation.

Training schedules

The most fundamental principle in motor learning is that the degree of performance improvement is dependent on the amount of practice [9]. Practice at its simplest is just performing the same movement repeatedly. Although this may be the most effective way to improve performance during the training session itself, it is not optimal for retaining learning over time. As Winstein *et al.* state 'All too often we forget about the seductive and often misleading temporary changes in performance and take them to reflect learning when in fact, little persistence of that change is evident even after a short interval' [10]. It has been known for some time that practice can be accomplished in a number of ways that are more effective than blocked repetition of a single task (*massed practice*). A consistent finding in the literature is that introducing frequent and longer rest periods between repetitions (*distributed practice*) improves performance and learning. The second finding is that introducing task variability in the *acquisition* session improves performance in a subsequent session (*retention*) even though performance during acquisition may be worse than if the task were constant [11]. A hypothetical example is reaching to pick up a glass on a table. The therapist can either have the patient reach and grasp the same glass at a fixed distance repeatedly or have the patient pick up the glass at varying speeds and distances. Although the patient may reach for the glass better during the constant session, the patient reaches for the glass better at retention after the variable session. Another benefit of variable practice is that it increases *generalization* of learning to new tasks. The idea of generalization is of critical importance to rehabilitation. Training subjects on a task repeatedly in the clinic may lead to improved performance in that particular task but not transfer to any activities of daily living (ADL) when they get back home.

Another robust finding is that of *contextual interference*: random ordering of n trials of x tasks leads to better performance of each of the tasks after a retention interval than if a single task were practiced alone [12]. So in the reaching example, the patient might reach randomly for a glass, then a spoon, then a telephone. There is a need to test efficacy of rehabilitation through tests of recall and transfer rather than performance at the time of training. In addition, the effects of practice schedule need to be applied to research on rehabilitation techniques and motor recovery after stroke. An example of such a study compared practice under conditions of contextual interference (random practice) and massed practice in patients with chronic hemiparesis. The patients who learned with random practice showed superior retention of the trained functional movement sequence [13]. The reason why a random schedule might aid recovery is that it promotes considering each movement as a problem to be solved, rather than a time of sequence of muscle forces to be memorized and then replayed. It is the goal not the movement that has to be repeated. When we reach for a glass of water we do so differently each time because of small differences in posture, position of the glass relative to the body etc. Nevertheless, a reach is always successfully achieved. Within the context of the practice schedule, it may be that the influential idea of a motor recovery plateau at 6 months after stroke reflects asymptotic learning after massed practice rather than a true biological limit [14••].

Motor learning in patients with hemiparesis

There have been surprisingly few studies of motor learning after stroke and almost none looking at deficits in motor memory formation despite the likely relevance of these processes to rehabilitation [15] and recovery [16]. Winstein and colleagues [17] tested the ipsilesional arm in patients with middle cerebral artery territory infarctions using an extension-flexion elbow reversal task on a horizontal surface with feedback given as knowledge-of-results. The authors found no difference in acquisition on day 1 or recall on day 2 between patients and controls although patients were less accurate overall. Only the ipsilesional arm was tested, however, so a learning deficit in the affected arm was not evaluated. A more recent study [18] showed impaired adaptation of the paretic arm to a laterally displacing force-field generated by a robot arm. Patients showed reduced capacity to make straight movements in the force-field and showed reduced after-effects. The authors concluded, however, that patients did not have a learning deficit *per se* but weakness-related slowness to develop the required force to implement anticipatory control. Thus, at the current time it remains uncertain whether there are specific motor learning deficits in patients with hemiparesis. There are a number of reasons for this. First, there have been too few studies. Second, there are many types of motor learning and they may be differentially affected depending on lesion location. Third, it can be difficult to demonstrate a learning abnormality in patients when performance is already considerably impaired at baseline.

Is recovery from hemiparesis a form of motor learning?

Longitudinal studies suggest that recovery from hemiparesis proceeds through a series of fairly stereotypical stages over the first 6 months post-stroke, irrespective of the kind of therapeutic intervention [19]. In particular, although there is heterogeneity in stroke severity and recovery across individuals, it has been shown that the time course of the change in the Barthel Index for patients with middle cerebral artery stroke is well fitted by a logistic regression model [20]. The model indicates that the earlier that patients show recovery, the better the outcome at 6 months and that the Barthel Index at 1 week explains about 56% of the variance in outcome at 6 months. A similar logistic regression was used to predict the likelihood of recovery of hand dexterity at 6 months, assessed using the action research arm test, in patients presenting with flaccid hemiplegia [20]. It was found that if patients failed to reach an arm Fugl-Meyer score of 11 or more by week 4 then they had only a 6% chance of regaining dexterity at 6 months. Notably, this probability did not change over the ensuing 5 months. Thus, there is a process of spontaneous recovery that is maximally expressed in the first 4 weeks post-stroke and then tapers off over 6 months. Several mechanisms are likely for this spontaneous recovery, including restitution of the ischemic penumbra, resolution of diaschisis, and brain reorganization. Although some aspects of brain reorganization are probably unique to brain injury, there are large overlaps with development [21,22] and motor learning [23,24]. A recent study in a rat stroke model demonstrates the critical interaction between rehabilitation and spontaneous recovery processes early after stroke [25]. Rehabilitation initiated 5 days after focal ischemia was much more effective than waiting for 1 month before beginning rehabilitation. This difference correlated with the degree of increased dendritic complexity and arborization in undamaged motor cortex. A similar time-window effect, albeit longer than in rats, has been shown in patients after stroke, with the greatest gains from rehabilitation occurring in the first 6 months [26].

Improvement with rehabilitation increases with the amount of training and relates mostly to the task practised during therapy, with little generalization to other motor tasks. Thus, recovery related to spontaneous biological processes seems to improve performance across a range of tasks whereas recovery mediated by training, like learning in healthy subjects, is more task-specific. This difference raises the important issue of true recovery versus compensation and how they both relate to motor learning. True recovery means that undamaged brain regions are recruited, which generate commands to the same muscles as were used before the injury. This implies some redundancy in motor cortical areas with unmasking, through training, of pre-existing corticocortical connections [27]. Compensation, in contrast, is the use of alternative muscles to accomplish the task goal. For example, a patient with right arm plegia can compensate by using their left arm. Nevertheless, despite the clear distinction, learning is required for both true recovery and compensation. Experiments in monkeys clearly demonstrate the importance of learning for recovery of function [28,29]. A subtotal lesion confined to a small portion of the representation of one hand resulted in further loss of hand territory in the adjacent, undamaged cortex of adult squirrel monkeys if the hand was not used. Subsequent reaching relied on compensatory proximal movements of the elbow and shoulder. Forced retraining of skilled hand use, however, prevented loss of hand territory adjacent to the infarct. In some instances, the hand representations expanded into regions formerly occupied by representations of the elbow and shoulder. This functional reorganization in the undamaged motor cortex was accompanied by behavioral recovery of skilled hand function. These results suggest that, after local damage to the motor cortex, rehabilitative training can shape subsequent recovery-related reorganization in the adjacent intact cortex. Critically, cortical changes may only occur with learning of new skills and not just with repetitive use [24]. It is unclear at this time whether simple repetition of a task that was previously well-learned is sufficient to induce significant cortical reorganization or whether patient should be challenged on more difficult tasks. The answer may depend on the amount of salient error information provided (see section below on virtual reality).

The ability to compensate for a deficit is also dependent on motor learning, as any right-hander who has tried to write with their left hand quickly realizes. Thus to the degree that all rehabilitation is a form of motor learning, it can occur to promote both true recovery and compensation. A recent study of focal cortical ischemia in adult rats suggests that motor improvement is mediated principally by compensatory mechanisms rather than true recovery. Indeed, some animals developed a compensatory movement strategy that was more successful than the one used prior to the lesion [30••]. Most interestingly, the rate of improvement with training was similar before and after the lesion, suggesting that a similar learning mechanism was operative with and without injury. Another recent study of focal ischemic brain injury in rats suggests that the undamaged (ipsilateral) hemisphere may be the anatomical substrate for compensatory improvement [31]. These animal studies indicate the benefits of detailed behavioral analysis. Unfortunately, outcome scales commonly used in clinical rehabilitation trials do not have the resolution to distinguish between compensation and true recovery. This is a serious limitation for a number of reasons. First, it has been stated that the failure of many recent clinical stroke trials may relate more to the choice of outcome measures rather than to the lack of efficacy of the agent under investigation [32]. Second, inappropriate compensatory strategies may limit recovery after stroke [33]. Third, in order to understand brain changes that occur in response to therapy it is imperative that brain changes due to compensation are not misinterpreted as evidence for reorganization. The application of quantitative movement analysis and the motor control framework described in the previous sections should overcome these limitations and allow accurate assessment of the efficacy of rehabilitation techniques.

Rehabilitation methods based on motor learning

This section will review five rehabilitation techniques based on motor learning principles. Some target patients with a particular degree of hemiparesis while others are appropriate across the spectrum from mild hemiparesis to hemiplegia. It can be envisaged that patients could be tried on the techniques in combination or graduate from one to another as they improve.

Arm ability training: impairment-oriented training for mild hemiparesis

This technique was developed for patients with mild hemiparesis [34], who complain of clumsiness and decreased coordination even though they may have normal neurological examinations and arm Fugl-Meyer scores. Deficits may only be apparent with more sensitive kinematic testing [35]. These patients, however, are the most likely to return to work after their stroke and so their deficits, albeit mild, can be devastating, for example, for electricians, hairdressers, or musicians. The arm ability training tasks were chosen based on a factorial analysis of different abilities in healthy subjects: hand grip, finger individuation, arm-hand steadiness, aimed reaching, tracking, and wrist-finger speed. The protocol incorporates many of the concepts from the motor learning literature in order to maximize retention and generalization of what is learned during the rehabilitation session. For example, although tasks are practiced repetitively, variability is introduced by varying the difficulty of each of the tasks. A randomized clinical trial showed a benefit of arm ability training compared with standard rehabilitation, as assessed by a measure of efficiency of arm function in ADLs [34]. The emphasis of the arm ability training protocol focuses on impairment rather than on disability or quality of life measures is more congruent with neuroscientific findings, which indicate that motor control and motor learning are modular [5].

Constraint-induced movement therapy (CIMT)

This technique has garnered a large amount of attention because it has shown that even patients with chronic stroke (> 6 months out) can show meaningful gains (for a recent review, see [36]). The technique has two components and is usually given over 2 weeks: (i) restraint of the less-affected extremity for 90% of waking hours; (ii) massed practice with the affected limb for 6 hours a day using *shaping*. In patients with chronic hemiparesis, the restraint is conjectured to help patients overcome *learned non-use*, whereas in patients with acute stroke it can be seen as a way to prevent adoption of compensatory strategies with the unaffected limb. Shaping is a form of operant conditioning whereby performance is consistently rewarded – essentially the reverse of the mechanism by which patients are posited to learn non-use. Learned non-use is based on the idea that the affected limb has potential ability that is unrealized because of excessive reliance on the unaffected limb. To be eligible for CIMT, patients must have at least 10° of wrist and finger extension. Several studies have now been published showing a significant benefit for CIMT in patients with chronic hemiparesis [37–39].

CIMT, however, remains controversial [40,41] and a number of issues still need to be resolved. First, the restraint is frustrating and there is preliminary data showing that massed practice alone can yield a significant benefit [42]. Second, the greatest benefit is seen when outcome is measured by the motor activity log. This is an ordinal scale from 0–5, which requires patients to assess their performance on motor ADLs, both in terms of how much they use the affected arm compared with the unaffected arm and on the quality of their movements. Less benefit is seen when impairment is measured. This discrepancy has been explained by Taub and colleagues as evidence for learned non-use: the patients who benefit the most are those who can move the limb well but do not out of habit [36]. This is unconvincing because it suggests that the restraint alone should have a large effect when most investigators believe that it is the intense daily therapy that accounts for the largest part of the effect of CIMT. Third, to be eligible for CIMT, patients must have at least 10° of wrist and finger extension, thereby excluding many patients. Fourth, it has recently been reported that intense rehabilitation (not CIMT) in the acute phase after stroke has little impact on ADLs 4 years post-stroke. Thus, it would be surprising if 2 weeks of treatment could have long-lasting effects either when administered in the acute or chronic setting. So far, patients have been followed out for 2 years with evidence for persistent benefit and those with greater impairment have a 20% reduction in motor activity log after 1 year [37].

Overall, despite the large amount of interest in CIMT, it still remains unclear what of type of recovery is actually occurring. A form of CIMT occurs when healthy subjects practice handwriting with their non-dominant hand. The improvement has been analyzed kinematically and it appears to occur at the level of individual strokes with true increase in skill, with decreased stroke duration and increased velocity without degradation in accuracy [43]. A similar detailed analysis needs to be done in patients to see if CIMT leads to a true increase in skill and whether this increase in skill is through use of a compensatory mechanism or true recovery. In addition, given what we have discussed about training schedules, it would be desirable to move away from massed practice over 2 weeks and see if more variable conditions of practice could be employed.

Electromyogram-triggered neuromuscular stimulation

Electromyogram (EMG)-triggered neuromuscular stimulation is based on sensorimotor integration theory, which posits that non-damaged motor areas can be recruited and trained to plan more effective movements using time-locked movement-related afference [44]. The critical importance of sensory input to motor learning was demonstrated in an experiment in monkeys, in which the primary sensory hand area, known to have dense connections with M1, was ablated [45]. The monkeys were able to execute previously learned tasks normally but were unable to learn new skills. Within this framework, recovery of function is analogous to acquiring a new skill. EMG-triggered neuromuscular stimulation involves initiating a voluntary contraction for a specific movement until the muscle activity reaches a threshold level. When EMG activity reaches the chosen threshold, an assistive electrical stimulus is triggered. A microprocessor connected to surface electrodes monitors the EMG activity and administers the neuromuscular stimulation. In this way, two motor learning principles can be coupled in one protocol: repetition and sensorimotor integration. A typical protocol is to have patients make 30 successful movement trials, for example, full range of wrist extension, 3 days a week for 2 consecutive weeks. A recent meta-analysis of EMG-triggered neuromuscular stimulation reveals that it is an effective post-stroke treatment in the acute, subacute and chronic phases of recovery [46]. Importantly, it has been shown that simple suprathreshold sensory stimulation, unrelated to movement, is of limited functional value [47]. EMG-triggered neuromuscular stimulation has also been coupled with two other behavioral interventions, each based on motor learning principles. The first of these was a randomized practice schedule testing the hypothesis that contextual interference will aid recovery [48]. The second was bilateral coordination training (i.e. mirror movements with the unaffected arm) [49]. These two studies are important because they applied findings from the motor learning literature to the design of rehabilitation protocols and because they show the benefits of combining two techniques simultaneously. It can be envisaged that patients with limited wrist and finger extension could be treated with EMG-triggered neuromuscular stimulation first in order to meet criteria for subsequent CIMT.

Interactive robotic therapy

The use of robot-induced force-fields to study adaptation to dynamic perturbations and growing awareness that motor learning and motor recovery share overlapping neural substrates, led to the idea that robotic devices could be developed to provide rehabilitation. Indeed, robot-assisted rehabilitation is an excellent example of how concepts from recent research in motor control can generate fresh thinking with regard to rehabilitation. The first robot rehabilitation trial used the robot to assist patients with an impedance controller when they made self-initiated planar reaching and drawing movements [50]. Assistive-therapy is congruent with the sensorimotor integration theory that underlies EMG-triggered neuromuscular stimulation. The patients initiate a movement and are then assisted to complete it and therefore receive reafference that can be related to the command and the movement. An advantage of the robot over EMG-triggered neurostimulation is that muscles across more than one joint can be assisted simultaneously. Subsequent trials have confirmed benefits in acute and chronic patients [51,52]. A study that compared robot-assisted therapy with intensive conventional therapy showed a significantly greater benefit of the robot on both measures of impairment and ADLs [53].

Robots can also be used to have patients adapt to novel force-fields, as has been done in healthy subjects. As discussed above, one study has suggested that patients with hemiparesis do not learn or implement new internal models as well as controls. Nevertheless, a force-field environment generated by the robot could challenge patients to learn an internal model in a varying environment. As we have already seen, a variable training schedule is better than a massed schedule as it promotes retention and generalization. One interesting approach has been to have patients adapt to a force-field that causes them to make directional errors that are even larger than usual [54]. In the adapted state, the patients revert to making their baseline directional errors. When the force-field is switched off, however, their after-effects reduce their baseline directional error. Whether this leads to lasting and generalizable gains or is just a form of trick remains to be seen. A final great advantage of the robot is that it provides a way to control and measure therapeutic efficacy of both robotic therapy and other rehabilitation techniques. Precise kinematic measurements can be obtained and, if patients are adequately constrained so that they cannot make compensatory trunk movements, it can be ascertained if true recovery, defined by the ability to make straight and smooth movements, can actually result from rehabilitation.

Virtual reality-based rehabilitation

Virtual reality (VR) is a simulation of the real world using a human–machine interface [55•,56••]. The equipment consists of a visual display, head-mounted or on a monitor; a motion tracking and/or force detection device; and augmented sensory feedback. Augmented feedback means that the feedback is more salient and selective than in the real world. For example, patients can have a virtual teacher in which properly executed arm movements are displayed in real-time along with the patient's own movements and the closeness of the fit between them given as a score [57]. Similarly, subjects can wear a cyberglove, which allows them to see a two-dimensional reconstruction of their hand with feedback about a particular aspect of its movement emphasized, such as the range of motion [58]. The VR set-up can be more or less immersive but completely immersive VR, in which the environment appears real and three-dimensional, can induce cybersickness. The main idea behind VR is attractive and plausible, namely that it can provide a varied and enjoyable environment in which patients can sustain the motivation to practice for extended periods of time and attend to specific components of error feedback. In essence, the patients are playing a videogame that rewards recovery with points. Nevertheless, the critical questions that need to be answered before investing in expensive equipment concern whether motor learning in a virtual environment generalizes to the real world and whether there are advantages of practice in a virtual versus a real environment. There is affirmative evidence for both questions in patients with chronic stroke, trained on VR tasks for the hand [57] and arm [58]. Although these studies are small and have not included controls, they highlight the potential of an approach that emphasizes principles of motor learning and then amplifies them in the VR environment.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 112–113).

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