CHAPTER 1

# Introduction

## *Current Approaches to Rehabilitation*

**SARAH A. RASKIN**



Perhaps the greatest finding in neuroscience in the past decade is that adult cortical representations are not fixed. Indeed, not only is there the possibility of cortical map plasticity and cortical synaptic plasticity, but is also appears that these mechanisms are responsible for learning. Research is only beginning to reveal the mechanisms that lead to plastic changes in the adult brain. However, recent literature on experience-dependent changes, including ones that are practice-dependent, can be used to inform future studies in motor and cognitive rehabilitation. For example, repeated use of a particular cognitive process during training should strengthen connections in the underlying neural circuitry and consequently should produce an increase in cognitive capacity. The aim for both cognitive and motor rehabilitation is that benefits should generalize to any unpracticed task that recruits the same underlying function; thus the ultimate goal is to produce improvements that are transferable beyond a controlled laboratory setting and can alleviate functional impairments in everyday activities. Toward this end, some rehabilitation researchers are beginning to use findings in plasticity to inform their research, and to use neuroimaging techniques to measure brain changes related to treatment.

Rehabilitation is generally thought of as comprising one of two types of interventions. The first type consists of interventions that target change

at the level of behavior (i.e., *behavioral approaches*); the second consists of those that target change at the level of restitution (i.e., *restorative approaches*). Behavioral approaches are thought to involve compensating for a function that has been lost, whereas restorative/restitution approaches aim to improve the lost function itself. In more recent years, a third category has been added: therapies targeting metacognition or self-regulation.

Teaching the use of external compensatory aids to prompt people to complete planned tasks at target times is an example of a behavioral intervention. Such interventions may also include teaching a new behavior or substitute skill (e.g., teaching persons with memory loss to make lists for shopping; teaching persons with hemiplegia to tie their shoes with their less affected arm exclusively) and/or an encouraging increase in time, effort, or both (e.g., more studying). An injured person may also adapt to a new situation by changing self-expectations, selecting new tasks, or relaxing the criteria for success. Whether people are taught to use a compensation or develop it on their own, they are active participants in its application.

Direct restitutive interventions use procedures that aim to improve or restore some underlying ability or cognitive capacity. Examples of restorative, impairment-based interventions include direct attention training (a drill-oriented therapy with hierarchical exercises designed to decrease attention deficits) and the administration of functional activities with the more affected arm to attempt to reestablish pathways affected by hemiplegia.

An example of a metacognitive approach is training people in the use of strategies or systems that facilitate self-monitoring during task completion. All three types of approaches—behavioral, restorative, and metacognitive—are useful as appropriate, and are generally used in combination.

Given these categories, it has been assumed that direct interventions are those most likely to lead to plastic changes in the brain. However, it should be remembered that brain changes can also be considered to be compensations or recovery. A *compensation* occurs when a noninjured brain region takes over the function of the injured region. True *recovery* involves improvement in function in an injured area. Thus, throughout this book, chapter authors discuss a wide variety of brain changes that have been measured and try to map these changes onto potential rehabilitation techniques, be they compensatory (behavioral), direct (restorative), or metacognitive.

In Chapter 2 of this volume, Kolb, Cioe, and Williams provide a basic overview of the mechanisms that underlie both cortical map plasticity and cortical synaptic plasticity. These authors have identified critical principles of plasticity that can be used to inform rehabilitation approaches. The first is that changes in the brain can be shown at many levels, including cellular, synaptic, systems, and *in vivo* levels. The second is that the brain can be altered by a wide range of experiences, and that experience-dependent changes can be long-lasting. The third is that training studies must be aware of the specific systems being targeted by the training and of how these sys-

tems react to experience such as the training procedures. The fourth is that experience-dependent changes interact. In addition, of course, some plastic changes reflect compensation while others reflect recovery, and the treatment must specifically be designed with one or the other in mind. In other words, in some cases the plasticity involves an intact cortical region's taking on the tasks once mediated by the damaged region. In other cases, it is now suggested, damaged regions can actually recover and resume previous functions.

The rest of the chapters in Part I of this book focus on experience-based cortical reorganization. First, Jones (Chapter 3) discusses changes observed in nonhuman animal models, particularly rodent models. She provides an important discussion of reactive synaptogenesis and neurogenesis, making the points that not all such connections are functional, and that functional connections take time to develop. She lays out the considerable evidence from her work and that of others for a lesion–behavior interaction, such that lesion-induced degeneration followed by training leads to the formation of new synapses and dendrites only in the cortex contralateral to the behaving limb. She also reviews the literature on enriched environments, demonstrating that these environments promote the capacity for future learning and may lead to behavioral compensation. Thus environmental stimulation may affect the degree of plasticity after brain damage. Furthermore, Jones raises important findings about the benefits and limits of both exercise and forced use before and after brain injury. One of her most important points is that brain damage may place the brain in a particularly dynamic state, where greater plasticity may be possible.

In Chapter 4, Nudo and Bury focus on the current evidence for motor and sensory reorganization in primates, including the plasticity of cortical maps in mature animals. They begin with a comprehensive discussion of dynamic changes in the receptotopic organization of cerebral cortex in response to injury, which they suggest is due to unmasking at multiple levels of the somatosensory system. They provide evidence that this process involves two phases. The first is unmasking due to the disinhibition of tonically suppressed inputs mediated by gamma-aminobutyric acid, subtype a (GABAa). The second, longer phase is dendritic sprouting, perhaps mediated by *N*-methyl-D-aspartate (NMDA). Thus, they provide a theoretical basis for both early and late plasticity following injury. They also raise the importance of context-dependent reinforcement, which certainly has ramifications for human treatment approaches. Another direct human analogy is provided in the comparison of postinjury repetitive motor tasks in nonhuman animals and focal dystonia in humans, including evidence for disorganized primary somatosensory cortex (S1) maps in musicians with dystonia. This finding has led to a theoretically based treatment with splinting to reestablish independent digit sensation and movement. This chapter then turns to the important work of Nudo and others on the dynamic nature

of motor maps in a series of seminal studies on motor skill learning and changes in cortical representation. Their exciting work using intracortical microstimulation suggests that compensatory mechanisms utilize unaffected cortical regions. One valuable lesson from their work is the importance of lesion size. That is, after a larger lesion, reorganization of adjacent regions may not be sufficient; therefore, reorganization may need to take place elsewhere in the cortex. They also document not just reorganization but novel postinjury connections formed through intracortical sprouting.

As this volume moves toward creating theoretical constructs to apply findings in neuroplasticity to the postinjury rehabilitation of humans, one of the important concepts to integrate is that of *cognitive reserve*. In Chapter 5, Stern not only reviews the considerable literature supporting the idea of cognitive reserve, but also explores possible explanatory mechanisms. This model has been used to explain why two people with similar lesion sizes may have widely different functional impairments. Cognitive reserve tends to be related to levels of intelligence, education, and occupational attainment. Thus, Stern points out, not only is brain reserve malleable by experience over a lifetime; these same lifetime experiences contribute to cognitive reserve and can affect recovery after brain damage. Cognitive reserve allows an individual with greater brain pathology to demonstrate symptoms and functional abilities equivalent to those of persons with a much lower degree of pathology. In a series of studies, Stern has demonstrated the possibility that individuals with greater cognitive reserve may be recruiting different network of brain regions to perform a cognitively demanding task—a form of neural compensation.

Chapter 6 is intended to provide a transition between the more theoretical experimental studies and those that are more clinical and applied. With my colleagues Mills and Garbarino, I look specifically in this chapter at practice-related changes in humans and research findings in humans, to suggest specific types of neuroplastic changes in response to experience in daily life. In particular, we note that the plasticity of motor and sensory systems may be different from that of cognitive functions. Training on sensory or motor tasks is most likely to result in an expanded cortical representation of the specific skills or processes required to perform the training tasks. In contrast, high-order cognitive tasks recruit a distributed network of regions whose activation is not determined by the specific sensory or motor requirements of the task. Consequently, increased efficiency of this network may be best achieved by increasing connectivity between regions and enhancing neural efficiency within regions.

Part II of the volume then turns to therapeutic approaches that take advantage of these findings. It begins with therapeutic approaches to motor functions. One area of treatment that has shown considerable promise is constraint-induced (CI) therapy. In Chapter 7, Morris and Bickel describe CI therapy, which is a prescribed, integrated, and systematic therapy

designed to induce a patient to use a more impaired upper extremity many hours a day for several weeks (depending on the severity of the initial deficit). Some of the important elements are that the therapy requires repetitive, task-oriented training for a significant period of time (several hours a day for 10–15 consecutive weekdays). The use of a generalization procedure to transfer gains made in the research laboratory or clinical setting to the patient's real-world environment is essential. Finally, the hallmark of this therapy is constraining the patient to use the more impaired upper extremity during waking hours over the course of treatment, sometimes by restraining the less impaired upper extremity in a mitt or cuff.

Morris and Bickel also review locomotor training (LT), which is an approach to gait rehabilitation that provides truncal support while giving manual sensory signals on a moving treadmill. Participants are supported in a harness over a treadmill. The theoretical basis for LT is that the spinal cord has the capacity to integrate the afferent input and respond with an appropriate motor output through a network of spinal interneurons. In one study, the amount of body weight support required was reduced from 40% to 0% over a period of weeks. Thus findings from both CI therapy and LT demonstrate that both of these treatments lead to functional generalization in daily life. In the case of CI therapy, these changes are related to plasticity in neural systems. In particular, these authors describe evidence for an expansion of cortical representation of the affected limb, altered cortical activation with movement, altered cortical excitation, and altered cerebral blood flow.

Part II then turns to approaches to rehabilitating cognitive functions. Chapters 8 and 9 deal with treatment of cognitive deficits in children. Chapter 8 focuses on developmental dyslexia, and Chapter 9 focuses on acquired attention deficits in children after brain injury. In Chapter 8, Shaywitz and Shaywitz ground their discussion of treatment in the well-supported theory of dyslexia as a phonological disorder. In a series of studies using functional magnetic resonance imaging (fMRI), these authors demonstrate differences in activation between children with and without dyslexia in areas of activation when the children are required to read words and pseudowords, pointing particularly to a dysfunction in left-hemisphere posterior regions. Moreover, they have been able to show compensatory changes in older children with dyslexia as compared to younger children with dyslexia, suggesting experience-dependent changes in brain regions used for reading.

Engle and Kerns focus in Chapter 9 on children with acquired brain injury, those with attention-deficit/hyperactivity disorder (ADHD), and those with cancer affecting the central nervous system (CNS). One of the main approaches described in this chapter is the process approach to attention training, including the Pay Attention! materials designed by Kerns and her colleagues. These materials are theoretically grounded in a clinical model of attention and demonstrate the need to focus rehabilitation efforts

on the specific aspect of attention that is deficient (e.g., sustained, divided, alternating). These materials are also hierarchically based, allowing for greater cognitive demand as an individual becomes proficient at each level.

In the chapter on rehabilitation of language deficits (Chapter 10), Leon, Maher, and Gonzalez Rothi describe an exciting novel application of the principles of CI therapy to language functions. Constraint-induced language therapy (CILT) is designed to eliminate the potential learned nonuse of speech in individuals with aphasia. CILT incorporates the principles of repetition, intensity, salience, and specificity of treatment. The idea of constraint in this case is the limiting of the person's responses to speech by using visual barriers that prevent any communication through gestures, drawings, facial expressions, or other alternatives to speech. The therapy is hierarchically organized so that at first only a single word is required, then full sentences, and so on. Results have suggested that improvements are generalized to daily life. In one study, CILT was demonstrated to be superior to Promoting Aphasics' Communicative Effectiveness (PACE) therapy.

The next two chapters focus on two different aspects of executive functioning. In Chapter 11, O'Connell and Robertson review the literature on targeted training of executive attention and working memory, including studies that have included people with brain injury and children with ADHD, in addition to studies of age-related cognitive decline. They review studies that have used imaging techniques to try to measure reorganization of cortical networks. They also discuss their own successful work using strategy training and self-instructional techniques to improve sustained attention.

In Chapter 12, Lillie and Mateer review more metacognitive executive functions, such as error monitoring, problem solving, and multitasking. These authors give solid practical suggestions for treatment, but do so within a context of caution due to a lack of current data. They point out several important considerations for remediating executive functions, including the multiprocess nature of most executive tasks and the need to improve overall cortical tone before executive deficits can be addressed.

In the final chapter on cognitive training (Chapter 13), Sohlberg and Ehlhardt Powell review the literature on instructional practice and make important connections to brain plasticity and remediation. These principles from direct instruction are useful across all cognitive domains, but are particularly important to learning and memory. Some specific aspects of learning and memory approaches that are discussed in this chapter are errorless learning and distributed practice-spaced retrieval. In particular, a treatment protocol developed by these authors and their colleagues called TEACH-M is described and reviewed.

In the final chapter of this volume (Chapter 14), Freeland discusses pharmacological therapies that have been designed to improve cognitive

or motor functioning. Many of these can be used in conjunction with non-pharmacological therapies to enhance recovery. Freeland makes the point that in most studies neuroplasticity is not directly measured, but inferred, and he urges researchers to begin examining neuroplastic changes as a theoretical guideline for creating new therapies.

Perhaps one of the most important factors in any rehabilitation approach is the need for generalization (Raskin & Gordon, 1992). One of the first authors to specify an approach to generalization was Gordon (1987), who suggested that the first level of generalization is that gains from rehabilitation hold true in the same setting with the same materials on separate occasions. The second is that improvement on the training tasks is also observed on a similar but not identical set of tasks. The third level of generalization is that the functions gained in training are shown to transfer to functions in day-to-day living. How does generalization occur?

Elsewhere, we (Sohlberg & Raskin, 1996) have suggested a set of generalization principles or strategies that can be broadly adapted to both research and clinical practice. These principles, drawn primarily from the applied behavioral literature (Stokes & Baer, 1977) and from the cognitive psychology literature on transfer or training (Anderson, 1996), are as follows: (1) Actively plan for and program generalization from the beginning of the treatment process; (2) identify reinforcements in the natural environment; (3) program stimuli common to both the training environment and the real world; (4) use sufficient examples when conducting therapy; and (5) select a method for measuring generalization.

These methods are thought to promote generalization through known learning and transfer of training paradigms. The process by which generalization occurs, of course, varies according to the treatment approach. Behavioral (compensation) techniques affect generalization by bypassing defective cognitive or motor functions and allowing a person to apply strategies in a large number of settings. Restorative approaches are thought to actually change the affected functions, thereby allowing the process to be more effective in any setting. However, the keys in any case seem to be to plan for generalization from the start and to have a measure of efficacy in place. In a meta-analysis of 39 papers on cognitive rehabilitation, Geusgens, Winkens, van Heugten, Jolles, and van den Heuvel (2007) concluded that a large number of studies make claims for transfer of training, but that relatively few actually evaluate whether transfer has occurred.

Some of the most exciting new work in the field of rehabilitation is based on models of cortical plasticity. Robertson and Murre (1999) have argued that the extent and nature of neural recovery following targeted intervention will depend largely on the severity of the injury. Thus, in the case of a large lesion, there may not be sufficient residual connectivity with

which to reestablish a fully functioning network. In these cases, then, treatment should be targeted at the compensatory recruitment of alternative brain regions or the use of compensatory strategies.

In a similar vein, there is some evidence to suggest that patients with brain injury require training tailored to their specific level of functioning. For example, an analysis of individual differences in a study of the Attention Process Training (APT) program (Sohlberg, McLaughlin, Pavese, Heidrich, & Posner, 2000) indicated differences in treatment efficacy, depending on a patient's initial vigilance level. Only individuals who had poor vigilance levels showed improvements in basic attentional skills after APT, and only individuals with better vigilance levels showed improvement on more demanding attentional or working memory tasks. Further work is required to establish predictors of training efficacy, and future studies should delineate specific patient profiles in order to determine who is likely to benefit.

Research in rehabilitation is increasingly being required to follow evidence-based guidelines, as it has been noted many times that such research tends to be limited by the heterogeneity of subjects, methods, and outcome measures. Although randomized controlled studies are assumed to provide the best evidence of efficacy, it is also accepted that in clinical practice it may be necessary to combine standard treatment protocols and individualized treatments (Cicerone et al., 2000).

As the field of neuroscience provides more evidence for the specific kinds of practice and experience-dependent learning that lead to the most effective cortical plasticity, it should also be possible to target rehabilitation efforts to maximize these potential changes.



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