# Cerebral Reorganization of Function After Brain Damage

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Harvey S. Levin
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I dedicate this book to Arthur Benton for the training I received under his leadership at the University of Iowa and for his mentorship throughout my career, to Robert Grossman and Howard Eisenberg for their encouragement during my transition to becoming an independent investigator, to Angela Williams for her support and understanding, and to Keisha S. Johnson for coordination with the authors and Oxford University Press.

H.S.L.

This book, like all my other research, is supported by the intellectual stimulation and care I receive from my wife Irene Litvan. To my mother, Phyllis, whose courage provided me the foundation that my career is built upon. Finally, I owe a great deal to all the staff and fellows who have passed through the Cognitive Neuroscience Section whose thoughts and creativity force me to continually challenge my own beliefs and methods.

J.G.

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# Foreword

Twenty years ago, a graduate student delving into the mysteries of nervous system injury or neurodegeneration understood the term *neuroplasticity* to refer to the developmental process and believed that after birth, it was downhill all the way. Today, a graduate student of neuroscience hardly knows where to begin to tackle the many processes that are involved in the dynamic, changing, responsive, "plastic" brain. Levin and Grafman have highlighted an exciting area of neuroscience from the important perspective of rehabilitation of the injured brain. The contents of this volume will lead the interested reader through the background, significance, practical applications, and potential future of neuroplasticity as a natural part of the living nervous system and as a tool to use in the treatment of neurological conditions.

The book has four well-rounded parts: a history and introduction, a perspective on the types of research relevant to brain plasticity, techniques to evaluate changes in the brain, and the possible applications of concepts of neuroplasticity to rehabilitation practice.

Parts I and II present a comprehensive and thought-provoking overview of the concepts of plasticity, or the capacity for change within the nervous system. Important theories in neuroscience and psychology are discussed in light of recent findings. The chapters in these two parts of the volume point out the usefulness of animal models, from rodents to primates, in the study of brain development, circuitry, plasticity, and injury. In addition to the existing paradigms, new technologies to produce knockout or transgenic animals will allow genetic dissection of the mechanisms that underlie the establishment of and changes seen in the brain's circuitry. These chapters present a wide variety of basic research that highlights important advances in neuroplasticity theory. Studies of primates show that alterations can occur in limbic cortical areas that control emotion, executive function, and reasoning capacities; it is intriguing to relate these observations to the sequelae of human traumatic brain injury. The intense connectivity among brain regions and the implications of these associations are clearly presented. Primate models certainly provide brain maps that can be closely related to human maps, and rodent models provide the opportunity for fairly rapid assessment of the numerous intrinsic chemical alterations that occur after injury. These factors change after injury, and such alterations may contribute to the molecular and synaptic plasticity that are part of regeneration and fiber sprouting in damaged systems. The observations of changes in cortical maps can be put into the context of changes in neurotransmitters, growth-stimulating proteins, and hormones. Several chapters present the robust responses of neurons and glial cells in a way that encourages further inquiry and adds important information to the knowledge base of any reader interested in neural plasticity, brain injury, or rehabilitation.

The authors do not shy away from the complexities of interpreting the findings from animal models of stroke and traumatic brain injury (TBI) that include attempts at treatment. Seemingly contradictory results from different models are reconciled by introducing important concepts relating to the possible cascades of secondary injury that result from ischemia and trauma and the timing of interventions meant to overcome deficits. For rehabilitation strategies, there may be periods of increased tissue vulnerability. Very early or aggressive programs of therapy may actually promote maladaptive plastic changes, leading to more severe lesions and deficits. The same cautionary note is applied to drug therapies, and agents that may appear efficacious when given soon after injury may do harm if therapy is delayed. These observations are important to both researchers and clinicians in the field who wish to design therapies for TBI.

The second half of the book provides both an excellent overview and detailed studies of plasticity in the human brain, both in the developing child and in the injured adult. These chapters present numerous methods of studying brain function that include neuropsychological tests and medical imaging. As one author states, "The developing brain is a dynamic, responsive, and self-organizing system. Early injury constitutes a perturbation of normal development" (Stiles, Chapter 10, p. 201). The effects of TBI, especially a mild injury, may not be immediately apparent, but emerge later during development when language, reading, or social interactions are usually acquired. The complexities of development and damage are often difficult to dissect. Again, the authors present the difficulties as well as the possible interpretations and caveats of using a particular parameter to assess function. Such methods as functional magnetic resonance imaging, electroencephalography, dichotic listening, and position emission tomography, scanning, to name only a few, are presented along with case studies of a variety of developmental disorders, TBI, and stroke. Results are interpreted carefully, with an understanding of the techniques used, the disorders under study, and the developmental processes that may impinge on results. Such a careful overview presents the reader with an idea of the combination of assessment tools that are necessary when tackling a study of brain plasticity. The discussion of future directions for research and practice presented in Chapter 19 provides an exciting conclusion to the volume.

The book leads the reader through the complexities and promise of neuroplasticity, and presents insights into current and future research and clinical practice. It is a valuable overview for anyone interested in how the brain works, develops and creates, responds to injury, and forms itself in response to the environment.

Mary Ellen Cheung, Ph.D.
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# Preface

It is compelling to watch a young child learn the meaning of a new word or how to play a computer game. Children learn through trial and error and at times demonstrate a remarkably rapid learning curve. Fortunately, learning is not restricted to children; we retain the capacity to learn throughout life. This capacity can even be seen when children and adults suffer brain damage and need to relearn knowledge or skills that they had previously acquired or need to learn new knowledge and skills. That the brain mediates this learning and is the storehouse of new knowledge and skills has been known for centuries. What has been less certain is how the brain manages to change to accommodate new learning under normal conditions or following damage at various stages in development. Within the last 30 years, there has been considerable progress in forming an understanding of the genetic, cellular, assembly, system, and psychological factors that contribute to learning and plasticity. The purpose of this volume is to provide an update of much of that work and to suggest ways in which the knowledge gained in the laboratory can be translated into practical gains in helping people recover from brain damage.

Although it is clear that plasticity can be reflected at various levels in the nervous system, it is by no means obvious which level is most important or appropriate for an understanding of different forms of learning. The dominant theme in this volume is that changes at the network level are crucial for an understanding of how new learning is accomplished. For example, some researchers believe that the capacity to learn is reflected in the density of connectivity (and neurons) in a network. There is also evidence that as a network is activated and used during learning, the boundaries of the network expand to reflect its growing participation in a functional activity. The idea of a flexible boundary is appealing because it suggests that while the brain has regional functional networks that become firmly established at maturity, their boundaries can be extremely flexible in childhood and even in adulthood. It is not known whether this functional map expansion comes at a cost to the functional capabilities of neighboring networks.

One of the goals of this volume is to understand whether the basic principles of neuronal plasticity such as those described above can be used to develop treatments that can facilitate recovery of function after brain injury. There appear to be at least four major forms of neuroplasticity that can occur after brain damage. One form was alluded to above and is indicated by an expansion in the size of the cortical map of a sensorimotor or cognitive function with use. Another form of plasticity concerns the apparent transfer of function from one region of cortex to another—usually to the contralateral cortex. This phenomenon is generally known as *homologous region adaptation.* It suggests that the transferred function was at least partially latent (and perhaps inhibited or masked) in the homologous region and could not emerge without concomitant brain damage in the contralateral hemisphere. A most dramatic form of functional plasticity, known as *sensory substitution,* indicates that a cortical region previously devoted to accepting the sensory input of one modality (e.g., vision) is now capable of processing a new kind of sensory input (e.g., tactile information). This form of sensory substitution has been documented in subjects who were blind from birth and whose visual cortices, area V1, now serve as a relay station for the tactile information used in Braille reading. The fourth form of neuroplasticity is compensatory and can complicate the interpretation of observed learning and plasticity in people recovering from brain injury. In this case, an alternative mode of processing is now used to accomplish a task that was previously performed by the damaged area of the brain. For example, many people rely on spatial cues to navigate a route. If they incur brain damage to the nondominant parietal cortex, they may be left with persistent spatial-cognitive deficits. In order to navigate routes, they may have to learn to rely on verbal instructions. Using verbal instructions, they still may be able to achieve their goal (to reach a location), but it will be via an alternative cognitive strategy. No doubt the use of this compensatory strategy results in an altered distributed neural network, but rather than the emergence of a new function, it is the reordering of weights in the previously established distributed network that accomplishes the task. These four kinds of functional and neural adaptation (of the brain) can be explored with a variety of tools ranging from single-cell and cell assembly recordings to functional neuroimaging techniques in humans. The advantages of any research effort are that the research at various levels of the nervous system proceeds in parallel and that the results obtained across levels can be integrated to achieve new insights.

Our desire to address these broad issues led to the organization of a workshop on neuroplasticity that was held at the National Institutes of Health in Bethesda, Maryland, and a series of lectures presented at Baylor College of Medicine in Houston, Texas. The chapters in this book are an outgrowth of the talks given at these two venues.

We want to thank Dr. Mary Ellen Cheung of the National Institute of Neurological Disorders and Stroke for her support and encouragement in organizing the workshop on neuroplasticity, which was held on the campus of the National Institutes of Health in Bethesda, Maryland. We also want to thank the late Dr. Sarah Broman for her critical comments on the organization of the workshop, as well as Jeffrey House and Fiona Stevens of Oxford University Press for their encouragement during the preparation of the book.

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*August 1999*

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# Cerebral Reorganization of Function After Brain Damage

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# 1

# Historical Notes on Reorganization of Function and Neuroplasticity

ARTHUR BENTON AND DANIEL TRANEL

## The Birth of Concepts

*Spontaneous recovery* of function after a disabling injury or illness must have been quite evident to observers since time immemorial. Early physicians and natural scientists had no great difficulty accounting for the phenomenon. Both natural and supernatural forces were considered to be quite capable of determining the course of disease, for better or for worse. Thus Hippocratic medicine generally ascribed unexpected recovery to the "healing power of nature" (*vis naturae medicatrix* in the Latin terminology). "Nature is the healer of disease. . . . It is nature itself that finds the way; though untaught and uninstructed, it does what is proper" (*Epidemics* VI, 5; cited by Neuburger, 1926, and Castiglione, 1958). Through the ages, the large element of truth in this doctrine has been amply confirmed. Neuburger (1926) provided a detailed account of its promulgation and interpretation by leading figures in medicine from antiquity to the middle of the 19th century. The recent rise of alternative medicine, which is striving in some cases for more or less equal footing with conventional medicine, is another testimonial to the power of this position.

Reliance on the efficacy of supernatural forces as a determinant of the outcome of illness dates back even earlier. And as the worldwide prevalence of faith healers and of prayers and supplications offered on behalf of the sick attests, this belief is still firmly held.

In the early 19th century a more specific factor was introduced by the French physiologist Pierre Flourens. This pioneer of the ablation experiment insisted that the cerebral lobes operated as a whole, without specialization of function in any particular region. All parts of the lobes (of the hen and the pigeon!) subserved all perceptual, intellectual, and volitional functions equally. When the lobes were completely removed, all of these capacities were completely lost. Ablations that were very large, but not complete, resulted in impairment, but not complete loss, of