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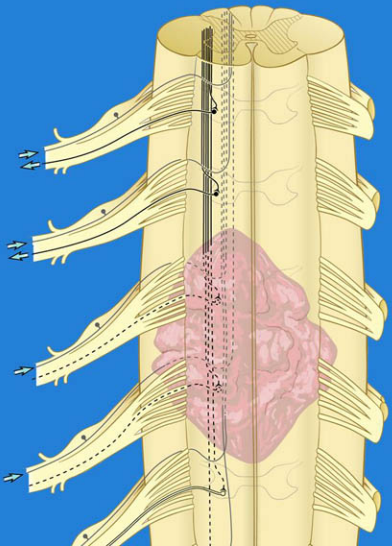
Restorative Neurology of Spinal Cord Injury



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This book is dedicated to Vivian L. Smith (1908-1989), founder of the Vivian L. Smith Foundation for Restorative Neurology, Houston, Texas, USA. Thanks to her continuous support and the understanding of William Butler, MD, then President of Baylor College of Medicine, the Division of Restorative Neurology and Human Neurobiology was created within the college (1987-1996). The Division housed clinical and research programs from which many new assessment and restorative treatment strategies emerged to help people suffering from weakness, paralysis, spasticity, or pain. This Division also trained many clinicians from around the world who have gone on to install the principles of Restorative Neurology into their own clinical and research environments to improve the quality of life for people who have suffered the effects of neurological injury or disease.

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FOREWORD

This is a textbook that has opinions, so be prepared to be pleased or irritated depending on your prior views. Hopefully, it will change at least some of these. The authors are pragmatic from the start. Despite the huge surge of interest in high technology solutions to SCI, such as spinal repair or brain machine interfaces, they recognize that these will take several more years to develop and may fail to yield as high an expectation as is sometimes portrayed. They concentrate squarely on current problems of individual patient management, always stressing the need to assess patients' remaining functional capacities with the greatest care possible. In particular they emphasize the so-called "discomplete" lesion, in which there may be no clinical sign of volitional control of muscles caudal to the lesion yet in which careful EMG monitoring may reveal activation of small numbers of individual motor units, or where volitional input can change spinal reflexes below the lesion. Both are signs of remaining connectivity and the authors highlight how these can be harnessed with appropriate techniques.

The approach is always to base treatments on remaining functional capacity in order to exploit the remarkable capabilities of the existing spinal circuitry to control function. The intrinsic circuitry of the spinal cord together with its sensory inputs and motor outputs is a remarkable machine that can produce fully functional patterns of motor output. The authors view this machinery as a "spinal brain" that can operate in a variety of different modes depending on the patterns of input that it receives. In this view, which reflects that of the neuroscience community at large, descending commands from the brain do not consist of patterned sets of instructions for individual movements and muscles, but are "biases" or "presets" that tune spinal circuits to operate in different modes and produce required patterns of output. The most remarkable demonstration of this is the spinal stimulation method pioneered by Dimitrijevic in which stimulation of the lumbar dorsal root inputs at different frequencies can result in different patterns of output to leg muscles varying from cocontraction to alternating "gait-like" patterns at other frequencies. Thus, just by changing the frequency of an input, we can change the pattern of motor output that is obtained.

The recognition of the intrinsic abilities of the cord below a lesion leads to the conclusion that more invasive interventions such as baclofen pumps or botulinum toxin, or even surgical intervention, must be used in a way that opens possibilities for control rather than simply for treating symptoms.

The chapters cover material from both the basic science perspective as well as the practical approach to treatment. The former contain sections on spinal locomotor generators in different species and discussions on possibilities of new treatments involving techniques from spinal regeneration with stem cells to nerve grafting. The latter cover the examination of remaining function as detailed in the Brain Motor Control Assessment (BMCA) Protocol and the individual approach to patient care. In addition there are sections on surgical monitoring of spinal function, on surgical prevention of early complications of injury and on functional electrical stimulation from neuromuscular stimulation to spinal cord stimulation.

Throughout, the emphasis is on remaining capabilities of the damaged system and developing methods to maximise its potential for restoration of function. The spinal cord itself contains the best circuitry for control of our muscles, and only by harnessing that in the most effective way will we be able to optimize individual patient function.

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PREFACE

Today, between 721 and 1,009 people per million in the United States are estimated to be living with a spinal cord injury (SCI), and each year, 20 to 50 per million more are newly injured.[1] Significant progress has been made in the development of treatments for spinal cord injuries, prevention of medical complications, and improvement of mobility and independence. Today, patients with SCI have a similar life expectancy to that of non-injured people. Rehabilitation engineering and robotics continue to develop devices that enhance the ability of people with SCI to perform activities of daily living, participate in community activities, and achieve a better quality of life than was possible even 10 years ago. However, these methods and devices have been designed to replace lost movement rather than to take advantage of and strengthen surviving, residual neural control of movement that often exists caudal to the injury.

Parallel studies of motor control in animals and humans have contributed to our knowledge of how the central nervous system generates and controls movement. In animal models of SCI, studies examining neurons and the circuits they form, the loss of connections between nerve cells, and the processes by which anatomical and neurochemical reorganization occurs after injury have told us that recovery is a complex and dynamic process that begins in the acute phase and continues throughout the patient's life. Furthermore, findings from these animal models have begun to suggest and test potential interventions to protect and restore neural circuitry affected by SCI. Thus the stage has been set for treatment of SCI in humans to transition from replacing mechanical function to restoring neural control of movement. However, in order to accomplish this paradigm shift successfully, it is essential that we recognize and respect the neural circuitry that survives after SCI.

The development and application of neurophysiological assessment methods in humans with intact and damaged central nervous systems have made it possible to advance our understanding of the nature of neural circuits that produce reflexes and perform automatic and volitional movement. Thus, in human SCI, it has become possible to assess the features of altered motor control below the level of the lesion. This approach, the testing of neural circuits, has contributed to the translation of clinical neurological findings from the large variety of neurological motor deficits

1. Cripps, R. A., Lee, B. B., Wing, P., Weerts E., Mackay, J., Brown, D. A. "GA global map for traumatic spinal cord injury epidemiology: Towards a living data repository for injury prevention." *Spinal Cord*. Published ahead of print. DOI: 10.1038/sc.2010.14949(2011):493–501.

found in people with SCI into information about their motor control and the underlying mechanisms of its disruption.

The assessment of motor control below the spinal cord injury allows us to monitor the modified functional relationships within the hierarchical network of motor control in such a way that absent or partially preserved brain control over the lumbar locomotor network can be substituted for or improved by artificial external electrical control. This is only one of numerous examples where the newly established functional relationship between the brain and the lumbar cord can be modified by additional external control. Therefore, it was important to assess SCI-altered neurocontrol to determine the underlying mechanisms responsible for the changed performance and clinically unrecognized residual function in order to design appropriately tailored intervention strategies.

This approach to the treatment of spinal cord injury through the assessment and modification of surviving motor control has led to the establishment of a *restorative neurology* program for spinal cord injury that is described and discussed in this book. Emerging over the past 50 years, this program recruited established multidisciplinary teams to demonstrate the efficacy of such a clinical practice.

This book is written for health care professionals to provide them with theoretical and practical information about restorative neurology in spinal cord injury. Here, for the first time, we describe the underlying principles of restorative neurology in one comprehensive text. These principles are supported by a wide variety of clinical applications. For this purpose we invited active health care professionals and scientists to contribute their knowledge of and experience with the application of these principles in their specific fields.

This volume is structured into four parts. Part I is dedicated to the clinical practice of restorative neurology (Chapters 1–3). Part II deals with the experimental animal work that has been done on the neurocontrol of locomotion and repair of the injured spinal cord (Chapters 4–5). Part III focuses on practical aspects of reconstructive neurosurgery (Chapters 6–7). Part IV is devoted to the assessment of motor control in chronic and acute spinal cord injury and includes restorative methods that focus on the lumbar spinal cord network such as posterior root stimulation (Chapters 8–10).

In Chapter 1, Dimitrijevic introduces the concept that, following traumatic injury, spinal cord neural circuitry and its connections to and from supralesional centers are altered and highly individualized. He draws from his experience with a large number of patients who were neurophysiologically examined during decades of work on identifying and characterizing subclinical aspects of neural function while developing restorative neurology in Houston, Texas. In this chapter, he makes the point that, once physiologically characterized, this new anatomical organization created by the injury and biological recovery becomes available for selective, targeted intervention. He also stresses the clinical and subclinical criteria that need to be applied when examining the resulting "residual motor control" and the role of each in the selection and adjustment of restorative procedures applied to upgrade function in the chronic phase of recovery.

In Chapter 2, Kakulas, Tansey, and Dimitrijevic describe and discuss the specific clinical and neurophysiological principles that underlie the assessment of residual motor control caudal to a spinal cord injury in humans. They extensively describe clinical, laboratory, and neurophysiological criteria for recognizing subclinical

neurocontrol of movement in chronic spinal cord injury. This chapter also reviews published work that describes and supports the neurophysiologically differentiated "discomplete syndrome" that exists within the paralyzed, clinically motor-complete patient population. Finally, they cover the examination of motor control in gait and introduce the lumbosacral locomotor central pattern generator circuitry, its behavior and modification after SCI.

The third chapter in this section, by Tansey, Dimitrijevic, Mayr, Bijak, and Dimitrijevic, describes the clinical practice of restorative neurology using neurophysiologically based interventions to improve motor function in chronic SCI. They cover the specific treatment modalities used to adjust residual motor control and produce improved function, including: physiotherapeutic techniques; neuromuscular, functional, and spinal cord electrical stimulation methods; intrathecal and peripheral nerve pharmacological interventions.

In the second part of this book, Vrbová, Sławińska, and Majczyński (Chapter 4) present animal models of SCI and discuss how an understanding of the mechanisms responsible for producing the locomotor pattern, rhythmic limb movements associated with locomotion, is useful for the development of interventions to repair the damaged spinal cord. They provide an extensive review of the work performed in cat and rat models of SCI describing the contributions of supraspinal, spinal, and peripheral neural circuitry to the generation of spinal motor output, organized to perform functional standing and stepping movements. Their review includes models of complete transection, selective focal lesions, and generalized diffuse injury and covers the effects of a wide array of ablative and pharmacological manipulations. Finally, they review what is known about the different neurotransmitter systems at work in the spinal neural circuitry and how they are impacted by SCI.

In Chapter 5, Vrbová and Sławińska explore recent intervention approaches being tested on patients in relation to the experimental work performed to encourage regeneration within the central nervous system. They review studies that have elucidated the neurobiological basis for the difficulties faced by neurons attempting to survive, grow, and interconnect within the damaged spinal cord. Their comprehensive review includes results from studies that examined the success of neural grafts made from a wide variety of cell types and sources that have been implanted in attempts to replace lost cells and bridge lesions within an array of support strategies.

The next part of this book focuses on the surgical treatment of chronic SCI in humans. In Chapter 6, Brown describes "reconstructive" neurosurgery as the functional neurosurgical counterpart to restorative neurology and reviews its use in SCI. He presents a conceptual framework for understanding the "new anatomy" caused by trauma to the spinal cord and how interventions must capitalize upon its unique features. This chapter covers neurosurgical methods to reduce spasticity and augment function in upper and lower limbs by decreasing pathological input to spinal motor structures. It also covers peripheral nerve and tendon transfer techniques and treatment to improve control.

Tansey and Kakulas review, in Chapter 7, the pathophysiological status of the spinal cord after injury and establish criteria for biological intervention. They detail the pathological cascade that occurs during the acute phase of the injury in which damaged axons swell, excitatory neurotransmitters trigger excitotoxic injury, reactive oxygen species are generated, and inflammation develops, leading to further loss

of neurons and glia. They describe the application of agents to impede this cascade and reduce the damage expressed in the finally established lesion. This chapter also reviews the effectiveness of pharmacological agents and neuronal grafts and provides guidelines for what should be done for a patient with chronic post-traumatic spinal cord injury if neurobiological interventions are available.

The fourth part of this book begins with Chapter 8: by McKay, Sherwood, and Tang, in which they present the practical aspects of assessing human motor control and describe changes caused by spinal cord injury. It focuses on the use of spinal motor output, recorded as surface electromyographic activity from multiple muscles during specifically selected reflex and volitional motor tasks to develop a profile of surviving motor control. This chapter is supplemented by Appendix I, a manual for conducting the brain motor control assessment (BMCA) protocol. Expected multi-muscle patterns from non-injured people and disrupted patterns typical of those with SCI are described and quantification methods presented that offer a sensitive, validity-tested method that generates a reproducible profile of motor control. The profile produced is then available for use in clinical research, and evaluation of changes in motor control induced by treatment.

In Chapter 9, Deletis, Sala, and Costa provide detailed descriptions of methods used for the intraoperative neurophysiological assessment of spinal cord function, including the epidural, scalp, and electromyographic recording methods, to evaluate ascending and descending long-tract conduction. They review the neurophysiological, killed-end potential that indicates the site of traumatic injury and markers that have been established as indicators of transient and permanent surgically induced loss of function.

Chapter 10, by Minassian, Hofstoetter, and Rattay, describes the selective stimulation of posterior root fibers through surface electrodes to produce reflex responses recorded from multiple muscles. They discuss the use of these responses that, like H-reflexes, are used to monitor changes in spinal motor excitability resulting from conditioning stimuli or motor task attempts, in the assessment of post-SCI function. Finally, they describe the use of this noninvasive transcutaneous approach to modify spinal motor control that is being expressed as spasticity and thus, to improve function.

Much of the work presented in this volume and the concepts that underlie the definitions and principles of restorative neurology are the result of contributions made by many individuals working in many laboratories around the world. It relies heavily on the development of tools that measure electrical activity and neurophysiological methods for examining the neural circuits in humans that has occurred over nearly a century. Appendix II by Zupanič Slavec provides the historical context in which the perspective presented in this book was developed.

The book concludes with an epilogue, prepared by Andresen, Kakulas, Vrbova, and Dimitrijevic, which critically evaluates the significance of considering residual neural function at the subclinical level in clinical practice to enhance the control of movement after spinal cord injury.

The development of this neuroscientific approach to human motor control after spinal cord injury was made possible by the continuous support of foundations for research and science in Slovenia, United States, Austria, and Norway. We would like to thank Craig Panner and Kathryn Winder from Oxford University Press for their continuous support while working on this book. We would like to express our

appreciation to Dr. Meta M. Dimitrijevic for her development and successful application of the clinical practice of restorative neurology. We would also like to thank Dr. Martin Grabois for maintaining a place for restorative neurology within Baylor College of Medicine in Houston, Texas, USA. A special expression of gratitude is owed to Dr. Heinrich Binder for many fruitful discussions. Also, we appreciate deeply Kent Waldrep and his National Paralysis Foundation for always being around to provide creative, intellectual, and financial support to sustain the development of Restorative Neurology for spinal cord injury. The editors are also grateful for the efforts of assistant editor Simon M. Danner, who made this otherwise complex endeavor fluid and coherent. Finally the contents of this book are a result of contributions made by many professionals from many disciplines, but most importantly, from the people with injured spinal cords who so willingly supported and joined us in our process of learning about the motor control that survived their injuries.

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1

Residual Motor Function after Spinal Cord Injury

MILAN R. DIMITRIJEVIC

CONTENTS

1. CLINICAL AND SUBCLINICAL FUNCTION

Spinal cord injury (SCI) divides the spinal cord, disconnecting, to varying degrees, the caudal portion from supraspinal structures that include the brain, brain stem, and cerebellum. When neural circuitry belonging to the motor system is involved, then we must focus our interest on residual motor functions, the abilities that survive, and how motor control has been altered. Residual motor control may produce clinically obvious movement or be subclinical, able to modify motor excitability in ways that are only recognizable through neurophysiological recording. Persons with SCI whose residual motor function can produce clinically obvious movements also experience subclinical alterations in control that are relevant to treatment planning and can only be identified through neurophysiological means. The existence of clinical and subclinical residual descending input to spinal motor processing centers also provides some of the biological resources needed for repair of the injured spinal cord and restoration of its function. Thus, neurophysiological assessment to illuminate the subclinical aspects of residual neural function and neurophysiological intervention targeting this surviving motor control are the essential components of "restorative neurology."

The ability to perform a desired movement depends on the residual motor control that is present after SCI. Figure 1–1 illustrates this relationship by showing the dependence between movement capabilities and the degree of residual brain motor control.

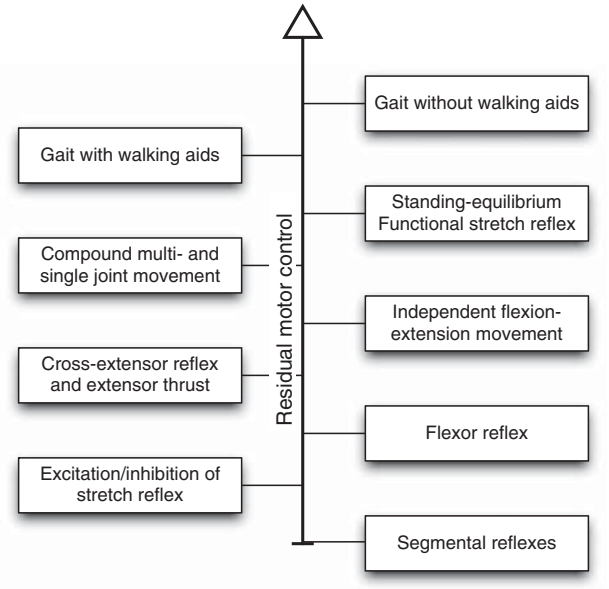

Figure 1–1 Motor capability depends on the degree of residual motor control.

Spinal reflex responses can be modified by residual brain influence: with an increase in brain motor control, more components of movement become available. For example, while weak residual control may provide only for whole-limb flexion-extension movement, greater residual control would support standing and walking.

Restorative neurological intervention would seek to augment residual motor control through external methods that increase the central state of excitability within the cord to enhance weakened brain motor control to improve function. This can be accomplished, for instance, by utilizing neuromuscular stimulation, functional electrical stimulation, and spinal cord stimulation.

2. NEUROPHYSIOLOGICAL ASSESSMENT—RESTORATION OF FUNCTION

Neurophysiology of human neurocontrol for volitional, automatic, and reflex movement and alteration of motor control after traumatic spinal cord injury has made significant progress in the past 20 years. Not long ago, manual muscle testing was the only method for assessing the severity of an incomplete spinal cord lesion (Little et al., 1990). Thanks to developments in human neurophysiological assessment of motor activity below the spinal cord injury, it has become possible, not only to assess clinical motor activity of incomplete SCI, but also to identify and record subclinical motor function (Eccles & Dimitrijevic, 1985). The possibility of adding subclinical, neurophysiogically recorded motor activity to the assessment of the spinal cord injured patient opened a new approach in the clinical practice of restorative neurology. Laboratory studies confirmed that subclinical residual motor activity can be used to augment basic excitatory and inhibitory CNS functions below the level of the

injury, thus enhancing motor control. The clinical practice of restorative neurology is built upon the subclinical discovery and measurement of residual function and the application of interventions that neurophysiologically enhance this residual motor control.

Injury of the multi-parallel system—the descending motor, ascending sensory spinal cord tracts, and spinal gray matter networks—results in altered or lost motor and sensory spinal cord functions. Months after the injury, between 10% and 20% of spinal cord injury subjects recover the ability to stand and walk (Ducker et al., 1983; Young, 1989). However, the rest may be wheelchair-bound, depending on their SCI and the degree of residual motor function present below the spinal cord lesion. The fact that residual motor functions are present in practically all chronic spinal cord injured people prompts the questions: how do we identify and characterize motor control; and then, how can this surviving control be externally modified?

3. SUBCLINICAL MOTOR CONTROL

An example, shown in Figure 1–2, illustrates how a patient recovered well-organized volitional activity for ankle movement five months after injury, and slightly improved motor control over the following years, even in the presence of paralysis in all other parts of his body. In the polyelectromyographic recording performed two and a half months after injury, there was no volitional activity, even at the level of motor units. Five months after injury, the beginnings of well-organized dorsal plantar flexion of the right ankle showed the return of volitional activity, and there were simultaneous clinical findings for traces of dorsal foot movement. During the next four months, the activity became organized, with increased amplitude, better reciprocity, and a

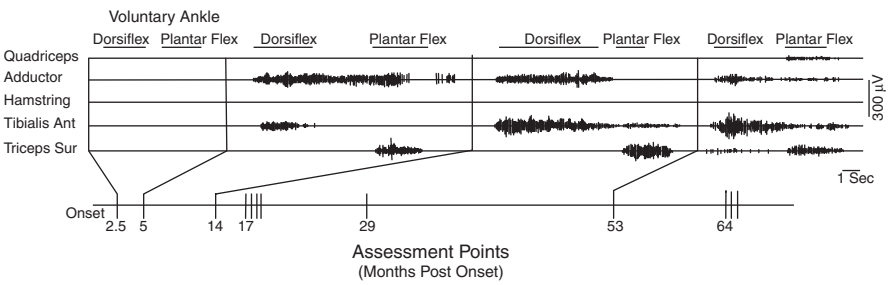

Figure 1–2 Recovery and improvement of volitional motor function in a quadriplegic patient. Four polyelectromyographic recordings of EMG activity recorded by surface electrodes from the right quadriceps, adductors, hamstrings, tibial anterior, and triceps surae muscle groups during the patient's attempt to perform ankle dorsal and plantar flexion (first recording 2.5 months after injury). Ankle movement task cuing is marked above the EMG traces. Calibration signal for EMG amplification of 0.3 mV is shown to the right of the figure. This figure summarizes the findings of 12 subsequent polyelectromyographic recordings acquired during 64 months, emphasizing that once volitional activity was recovered at five months after injury, it was maintained throughout the observation period (from Dimitrijevic, 1988).

more rapid onset and cessation of electromyographic (EMG) activity. These findings remained unchanged even after 14, 17, 29, 53, and 64 months, clearly illustrating that the right ankle had maintained the same degree of function throughout the observation period of five years.

In the clinically paralyzed leg, polyelectromyography can sometimes record volitional activation of motor units as illustrated in Figure 1–3, which shows the recording of attempted volitional activity in the same patient as was shown in Figure 1–2. Both lower limbs at that time were completely paralyzed. Two and a half months after onset, in contrast with the volitional clinical and neurophysiological activity present in the right ankle (Figure 1–2), the left leg recovered activity in isolated motor units in the adductor muscle groups, minute activity in the tibialis anterior and triceps surae, and the co-activation of the contralateral quadriceps, hamstrings, and triceps surae. The activation of motor units was subclinical, and there was no movement during this maneuver, but the patient described a feeling of stiffness.

When the patient performed preserved volitional activity of the right ankle (Figure 1–2), induced motor unit activity was present only in the right leg. However, when he attempted to move the left (Figure 1–3), minimal, subclinical EMG activity was present ipsi- and contralaterally, but there was no activation of muscles with residual volitional control. Therefore, the patient was able to generate motor unit activity in the absence of actual clinical movement and to maintain this ability for years. The patient in Figure 1–2 and Figure 1–3 also had incomplete impairment of sensory function immediately after injury. Three months later, a degree of recovery was documented, together with the presence of altered cortical somatosensory evoked

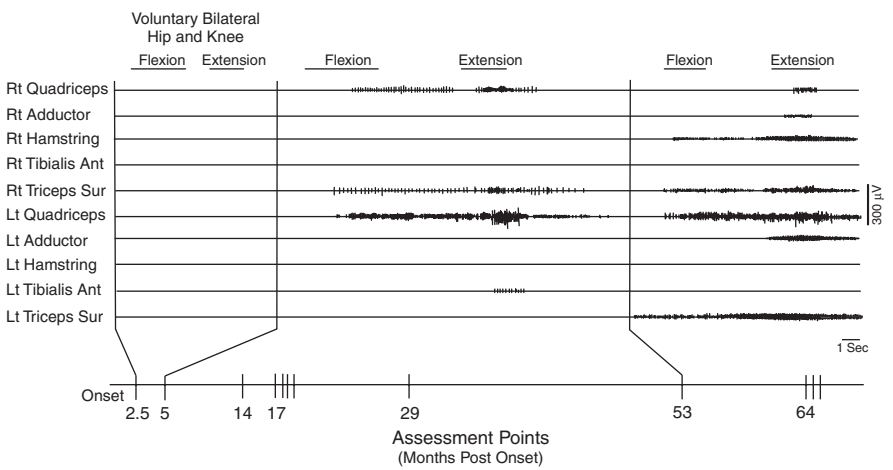

Figure 1–3 Subclinical improvement of residual motor function after SCI. Polyelectromyographic recording of motor unit activity during attempts to perform bilateral hip and knee flexion and extension. The patient was unable to produce any visible movement during the attempts. However, five months after injury, the patient activated the motor unit potential of 100 µV–150 µV, which was maintained four and five years following the onset of injury (from Dimitrijevic, 1988).

potentials from tibial nerve stimulation. Twenty-eight months after injury, sensory functions were nearly normal and were maintained throughout an observation period of seven years. Therefore, in this patient, the degree of injury to the sensory structures was less marked than that to the motor circuitry.

Analysis of this data showing the recovery of isolated and well-organized volitional activity for right ankle movement and the poorly organized motor-unit activation of the left leg, along with the nearly full recovery of sensory function, indicated that the ascending and descending functions of the central nervous system, which had been integrated before the onset of injury, were differentiated by the severity of the lesion, which resulted in different degrees and rates of recovery. These findings further illustrate that recovery of well-organized motor functions can begin even four months after injury. Therefore, nonfunctional recovery of suprasegmental control is also possible, and such residual influence can be present even in the absence of clinical activity.

Another example, which we studied at the end of the first week after onset of injury and repeated assessments throughout a year at regular monthly intervals, is the case of a gunshot lesion, which resulted in an immediate clinical neurological finding of a complete motor and sensory lesion of the spinal cord. Within the first week, the patient developed diffuse and severe muscle hypertonia, which persisted throughout the observation period. Within two months, the patient began to show signs of recovering sensory functions, but no clinically obvious evidence of motor recovery. However, the patient had preserved suprasegmental influence over segmental reflex excitability, and showed well-developed vibratory tonic reflexes and responses to reinforcement maneuvers in the paralyzed muscles of the lower limbs. Spasticity, in this case, developed within the first week after injury, so it could not be attributed to sprouting, synaptogenesis, or any other mechanism below the level of the lesion. It was probably caused by partial preservation of the descending facilitory and suppressive influence on lumbar spinal cord networks.

Residual central nervous system (CNS) axonal activity can help explain the clinical neurophysiological findings for subclinical evidence of brain influence in patients with clinically complete spinal cord injury. Therefore, by examining a large population of complete spinal cord injured patients, it might be possible to record the activity of single motor units in the corresponding, otherwise clinically paralyzed muscle groups that would be contracted during a specific motor task in subjects with intact CNS motor function. Actually, after examining 211 clinically completely paralyzed patients, this was found to be the case in six individuals, showing that volitional activation of only single motor units in paralyzed spinal cord injured subjects is rare, but possible. One of these six patients was able to activate very few motor units of the tibialis anterior when attempting ankle dorsal flexion, but a much larger number of motor units were activated when attempting a multi-joint flexion movement (Figure 1–4). The other five subjects showed a similar phenomenon of activation of single motor units during attempted dorsal or plantar ankle flexion, but only two of them had the ability to respond to multi- and single-joint volitional command with differentiated motor unit activity.

It was possible to repeat the above-described finding after several months and without training the subject to generate such motor unit activity through biofeedback or any other procedures. This suggests that, occasionally, in the fully paralyzed spinal cord injured patient, it is possible to document the function of the long

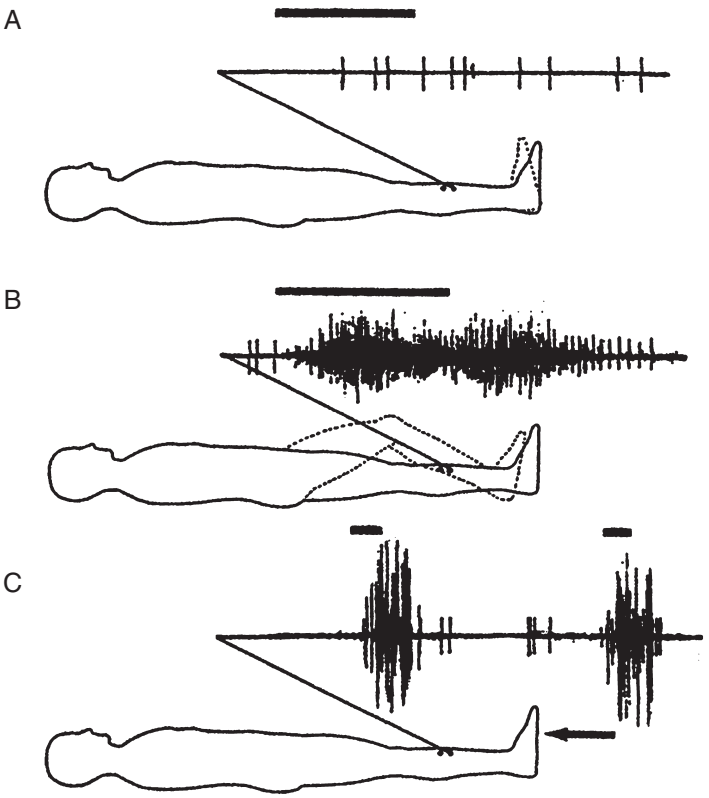

Figure 1–4 Rare finding of volitional motor control of single motor units in a clinically motor and sensory complete SCI subject. Summary of a recording with surface EMG electrodes from the right tibialis anterior muscle in a 19 year-old male, 42 months after onset of a C-5 spinal cord injury. Neurophysiological evaluation showed the presence of vibratory tonic reflexes and suprasegmental activation of motor units by reinforcement maneuvers. This particular patient was able to activate single motor units in the paralyzed tibialis anterior muscle when attempting dorsiflexion of the ankle (A). When he attempted to elicit multi-joint movement of the whole right limb (flexion of the hip, knee, and ankle), he was able to generate a much larger motor unit output (B). Plantar stimulation also activated the same tibial anterior muscle during a withdrawal flexion reflex (C) (from Dimitrijevic, 1995).

descending tract involved in the volitional control of isolated motor activity (Dimitrijevic, 1995).

Thus, if 10% to 20% of patients with traumatic spinal cord injury can expect a significant functional recovery, the remaining 80% to 90% will manifest numerous spinal cord dysfunctions with varying degrees of incomplete recovery.

4. EXTENT OF MOTOR CONTROL RECOVERY

In order to expand our knowledge of extended recovery after traumatic spinal cord injury, we examined 581 SCI subjects, both clinically and neurophysiologically

(Dimitrijevic et al., 1990). They were 116 women and 465 men whose time since injury ranged from two to 64 years. One hundred and eighteen of them were seen within the first six months after injury. Seventy were assessed between seven and 12 months, 111 between one and two years, 63 from two to three years, and 219 were assessed three or more years after onset. We were able to build three different illustrative groups. The first group consisted of 58 SCI subjects, whom we used for our clinical observation of their recovery. From those, 55 subjects showed evidence of motor complete spinal cord injury, and 13 of those 55 partially recovered and became motor incomplete after one or more years from initial injury.

The second group was composed on the basis of subclinical observations and consisted of 20 subjects who were initially motor complete, 12 of whom showed evidences for subclinical motor incompleteness by being able to activate motor units caudal to the lesion through reinforcement tasks or sustained response to vibration, or volitional suppression of withdrawal from plantar surface stimulation, five to seven years after injury. Thus, in this group, there was a large proportion of discomplete (see Chapters 2 and 8 and Appendix I) and incomplete subjects.

The third group is illustrated in Figure 1–5, which summarizes results of volitional multi-joint flexion and extension of lower limbs in six incomplete spinal cord injury subjects. We can see in this illustration that the strategy for performing this multijoint task was different when compared to subjects with intact nervous systems and across those with altered function due to the spinal cord injury.

Another group of 18 subjects was selected from the original 581 subjects because they suffered complete lesions and were studied two to three years after injury. Their neurological deficit had not changed, but they developed spasticity between one and 17 months after injury. Thus, there is no specific time window within which spasticity can appear in an initially clinically complete injury.

5. CONCLUSION

According to the observations described in this chapter, it is obvious that SCI produces a diverse population with a wide range of recovery that can occur years after injury. The majority of individuals with clinically complete lesions will, in time, regain at least some of their nervous system functions, even in the absence of clinical evidence of such. Others will reveal clinical signs of trace or gross but not functionally useful movement, while there are also some who can even recover the ability to stand and walk. Thus, in the majority of initially clinically complete SCI subjects, recovery of impaired functions can occur spontaneously, but the extent of this recovery varies. Therefore, surviving or residual motor control and that recovered after clinically complete SCI should be regarded as an available neurobiological resource for use in the restoration of spinal cord function and the upgrading of nonfunctional translesional interaction to a modest degree of functional motor control.

In summary, after SCI, residual brain motor function can develop with neurocontrol features that are quite different across individuals, and those features suggest the presence of conducting translesional axons and the locations of their endings within the spinal gray matter.

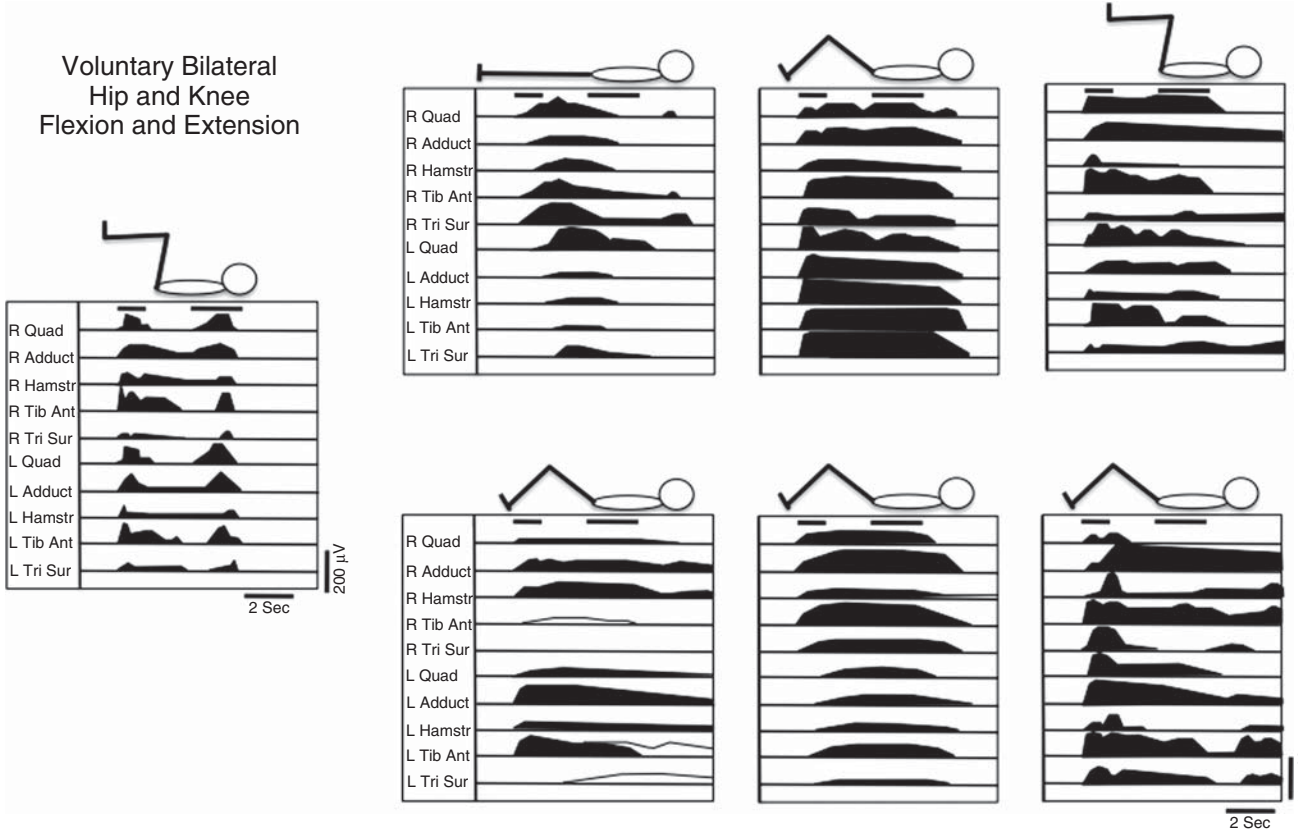

Figure 1–5 Schematic of EMG pattern recorded during the performance of a voluntary multi-joint motor task by a healthy subject (*left*). Three different SCI subjects (T8, C3, T7) attempt to perform the same task with different degrees of clinical movement (*top right*). Three other SCI subjects (T5, C6, C4) accomplish the same clinical movement with very different neurocontrol strategies (*bottom right*) (from Dimitrijevic, Lissens & McKay, 1990).

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2

Neurophysiological Principles for the Assessment of Residual Motor Control Below the Spinal Cord Injury in Humans

BYRON A. KAKULAS, KEITH TANSEY, AND MILAN R. DIMITRIJEVIC

CONTENTS

1. INTRODUCTION

The behavior patterns of spinal motor activity above and below a spinal cord lesion are diverse. The muscles below the level of the lesion, lacking varying degrees of volitional control, may show altered reflex, automatic, postural, and positioning regulation of the body and limbs. This altered spinal motor activity results in both loss of power, coordination, dexterity, and endurance (the so-called negative phenomena of paresis), and the emergence of uncontrolled and non-coordinated movements and/or muscular contractions (the so-called positive phenomena of spasticity). More often than not in spinal cord injury, it is not the presence or absence of movement that is the issue, but rather the quality and control of that movement. Fundamentally, the movements of normal stepping are similar to the movements in extensor or flexor spasms, but they differ in their magnitude, duration, rhythmicity, and modifiability.

Increased excitability of motor unit activity, exaggerated stretch reflexes, increased muscle tone, loss of cutaneo-muscular local responses. and impairment of volitional control are the sequelae of disordered or impaired supraspinal control and are collectively often referred to as the "upper motoneuron syndrome," or in clinical use, the "gestalt of 'spasticity.'" These effects are the more significant components of our noninvasive neurophysiological studies, which we have applied to patients with spinal cord injury (SCI) who show the clinical features of spasticity. The study of each of these phenomena contributes to our understanding of the neurophysiology of SCI. Our deeper, scientific understanding of these neurological abnormalities has been derived originally from animal experiments used to investigate the afferent and central mechanisms involved in mono- and polysynaptic segmental reflex activity. Lundberg (1967) described the contribution of different primary afferents and central inputs derived from the descending tracts, which converge on the spinal interneurons of the premotor network of the spinal cord (Dimitrijevic & Faganel, 1985; Dimitrijevic, 1987; Dimitrijevic, 1992).

Advances in animal neurophysiology, in parallel with the development of spinal cord neurology and human neurophysiology, have made it possible to introduce the assessment of motor control of the spinal cord below the level of lesion into the clinical practice of restorative neurology. Figure 2–1 illustrates the neurophysiological approach used for the assessment of spinal cord motor control in the human (Figure 2–1A).

Three major motor clinical syndromes are recognized in the human with SCI:

- Firstly, there is *incomplete SCI* with clinical evidence of altered but to some extent retained motor functions below the level of injury;
- Secondly, there is the clinical syndrome of *discomplete SCI* with absence of all voluntary motor function below the level of the lesion but with demonstrable neurophysiological evidence of residual conscious—i.e.,

volitional—influence upon spinal reflex activity below the level of injury;

- Thirdly, and the least common outcome of SCI, is the "absolute" *complete SCI syndrome* recognized as meeting all clinical and neurophysiological criteria for total absence of voluntary movement or sensation below the lesion and complete absence of any neurophysiological evidence of supraspinal influence or consciously directed influences on the spinal reflexes below the level of the lesion.

Figure 2–1 illustrates these three syndromes diagrammatically. *A* shows the impairment of transmission in the three syndromes. *B* shows the tests for stretch and cutaneo-muscular reflexes below the level of the lesion under specific paradigms with and without effort to elicit residual brain influence and volitional motor control. Depending on the severity of the lesion, additional assessment of volitionally controlled motor unit activity is reordered during the performance of motor tasks involving discrete and diffuse movements in order to delineate the features of altered motor unit activity resulting from the SCI.

In this chapter we describe the neurological and neurophysiological protocols for the assessment of motor control in the human spinal cord after injury and the basic principles applied when measuring an individual's spatiotemporal coordination of the activity of the motor neuron pools during reflex activity and volitional motor tasks.

2. PRINCIPLES OF NEUROLOGICAL EVALUATION

In the clinic it is common practice to carry out clinical assessment and classification of SCI according to the American Spinal Injury Association (ASIA)/International Spinal Cord Society (ISCoS) neurological standard scale (American Spinal Injury Association, 2002; Steeves et al., 2007). The ASIA classification is composed of the following:

1. The neurological level of the lesion based on volitional motor and conscious somatosensory (light touch and pain) testing
2. Whether it is clinically *complete* or *incomplete* SCI (loss or sparing of the lowest sacral levels' sensorimotor function)
3. ASIA impairment scale (AIS) Grade A, B, C, D, or E
4. Zone of partial preservation (ZPP) in complete SCI

Protocols for ASIA assessment are widely accepted and are the present tools used to describe the functional and clinical characteristics of post-traumatic SCI syndromes (American Spinal Injury Association, 2002).

Clinical neurological examination of motor function includes testing the maximal strength of volitional contractions, signs of neurological deficits in upper and lower motor neuron function, and corresponding clinical changes such as altered muscle tone resulting in spasticity and reflex changes secondary to the affected motor pathways.

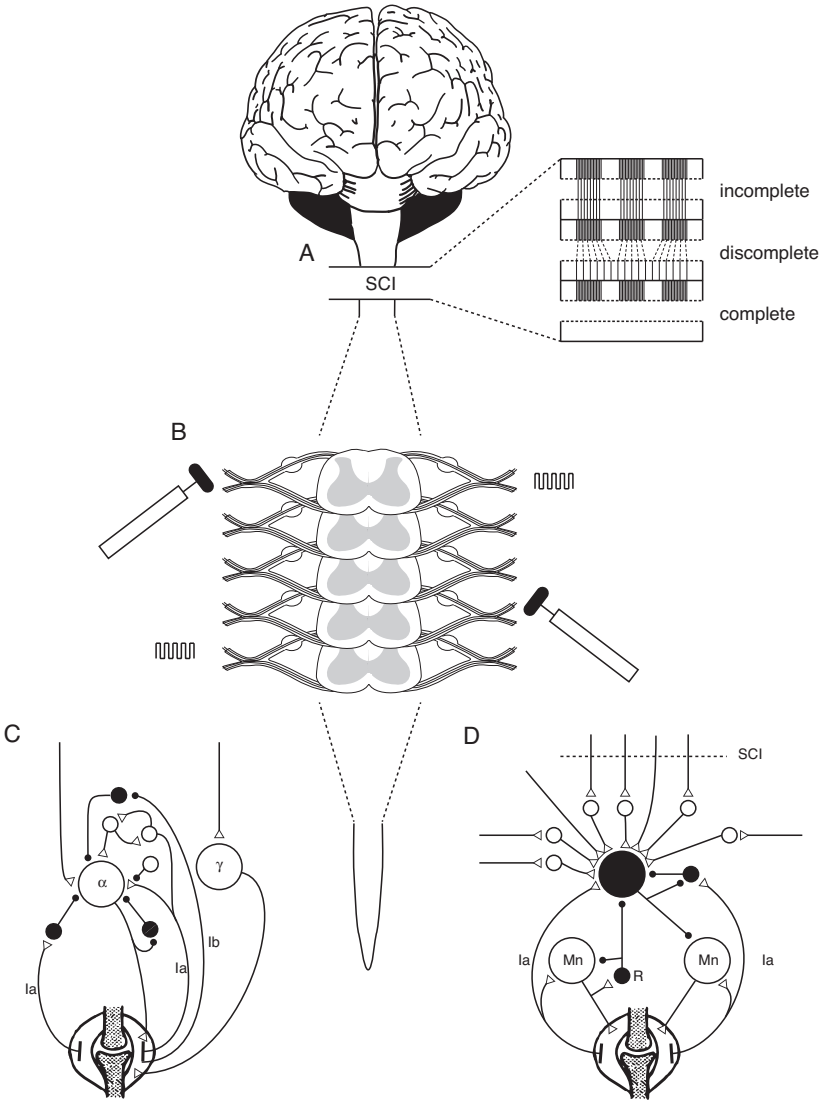

Figure 2–1 Sketch of (*A*) spinal cord injury, dividing rostral from caudal portions of spinal cord. (*B*) Sketch of plurisegmental networks illustrates simultaneous surface poly-EMG recordings of motor outputs during stretch, cutaneous-muscular reflexes, and brain-controlled motor task. (*C*) Sketch of circuits for stretch and cutaneo-muscular reflex. (*D*) Sketch of circuitry for premotor spinal cord center (adapted from Dimitrijevic, 1992).

Neurological definitions of *complete* and *incomplete* spinal cord injury syndromes were provided by Guttmann in 1976. The *complete* clinical syndrome included what was believed to be a clear-cut transverse spinal injury causing the complete loss of all voluntary and sensory functions caudal to the lesion. The *incomplete* clinical syndrome resulted when there was partial sparing of the spinal cord so that some

functions were retained below the level of injury. The incomplete designation was subdivided into two main subgroups: (1) a diffuse injury affecting more or less all of the central gray matter as well as the sensory and motor tracts again at any level but not resulting in complete loss of neurological functions below; (2) anatomically circumscribed lesions affecting distinct parts of the spinal cord resulting in incomplete deficits of dissociated type with the clinical picture being determined by which part of the spinal cord is involved as viewed in cross section. These incomplete syndromes are subclassified as being lateral, anterior, posterior, central, or mixed; or as pure motor, sensory, and cauda equina syndromes (Eidelberg, 1987).

However, our intention here is to draw the attention of the reader to several new clinical spinal cord injury syndromes that are based on neurophysiological criteria. First, in neurologically complete patients who supposedly have a transverse lesion of the spinal cord lacking all voluntary movement and conscious sensation below the level of the injury, we have identified individuals in whom neurophysiological evidence can be found of the transmission of signals passing though the injury zone. The resulting supraspinal influence on spinal motor function can be detected as changes in recorded patterns below the level of injury. These signals can only come from above, being induced either by conscious effort by the patient or by reflex-enhancing maneuvers such as neck flexion. This newly identified SCI syndrome may be considered to be subclinically incomplete. That is to say, there exists a spinal cord syndrome characterized by the retention of non-volitional residual brain excitatory and inhibitory activity with impulses traversing the lesion and thereby influencing reflex activity of the spinal cord below the level of injury.

We have coined the term *discomplete* to describe this new spinal cord injury syndrome, which can only be identified by neurophysiological assessments. Thus we point out that there are some patients who are thought to be clinically "complete" but who in reality are subclinically incomplete. This finding implies the theoretical supposition that there is a small population of axons that have survived the injury and are able to conduct signals through the injury zone. In this way properties of spinal reflex activities are modified by brain influence arising from supraspinal inputs (Sherwood et al., 1992). Neither the ASIA exam nor our neurophysiological assessments described above necessarily capture all supraspinal influences on infra-injury neural circuitry. For instance, it takes rather "complete" cervical lesions to release the phenomenon of autonomic dysreflexia, which probably reflects the loss of hypothalamic influence on preganglionic sympathetic neurons of the intermedial lateral cell column of the thoracic cord.

Considerable anatomical postmortem evidence exists in support of the concept of a clinically *discomplete* SCI syndrome as the phenomenon of the continuity of a small number of axons surviving the injury and passing through the lesion in an uninterrupted fashion is now well known (Kakulas, 1999).

The second, less-known, spinal cord syndrome is an *incomplete lesion with distinct biomechanical characteristics* resulting from diffusely distributed or patchy surviving and conducting axons of sufficient number to elicit similar alterations in reflex motor performance implemented through different motor tasks below the level of the lesion and showing neurocontrol features of functional muscle synergies (Dimitrijevic et al., 1990). Figure 2–2 is a sketch of these two new spinal cord injury syndromes: *A* showing a population of surviving, conducting axons which, during brain-controlled volitional effort, can modify the central state of spinal cord excitability expressed as

increased tone or as long-delayed involuntary movement and/or spasms below the level of the lesion; and *B* showing brain-induced volitional movement or the performance of a specific motor task eliciting a discrete or diffuse movement through activation of motor units—this being a feature of neurocontrol of so-called residual brain control in clinically incomplete spinal cord injury syndromes mentioned above and in Figure 2–2B.

Thus there are two situations wherein suprasegmental influences may be detected in otherwise neurologically complete SCI. The first is detected by surface polyelectromyography (sPMG) in the lower limbs when the SCI patient performs the Jendrassik reinforcement maneuver or makes some postural change; for example, neck flexion. The second is a change in tone and postural reflexes resulting from the same inputs and referred to as *biomechanical effects*. Both are due to a small number of descending axons traversing the injury site having survived the injury. The clinical and neurophysiological parameters of these discomplete syndromes correlate exactly with postmortem reports of humans wherein about a third of clinically complete patients were shown to have a small number of surviving axons in continuity from above to below the injury site.

These cases have been referred to as being *anatomically discomplete* (Kakulas, 1999). In these individuals, the number of preserved axons is insufficient for volitional movements or to conduct conscious sensation; that is, they are clinically complete, but nevertheless, residual axons are able to carry signals and influence the spinal cord below the level of the lesion, which manifest either as surface polyelectromyographic (sPEMG) changes or as biomechanical effects as described above.

In the clinical practice of restorative neurology, we have learned that it is essential to extend the neurological evaluation of upper motor neuron activity in SCI to include the following paradigms: (1) the stimulus-response paradigm to determine if the response to a test stimulus input is *present, altered, or absent;* (2) the conditioning paradigm in which peripheral or central input is added to determine if a response to a test stimulus can be modified and if so, by how much and in what ways and can the change be clinically observed; (3) repetitive task performance in which motor response behavior to stimuli delivered to the same site at a constant repetition rate, and strength of stimulation produce consistent responses, or do attempts to perform repeated volitional motor tasks produce identical movements or is there a the developing trend of increase, decrease, or disruption over time (Figure 2–3).

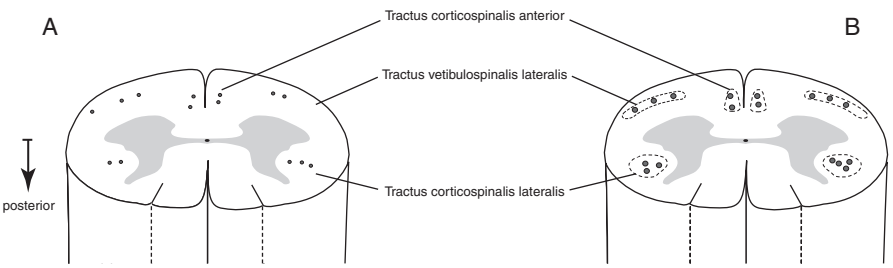

Figure 2–2 Schematic drawings of (*A*) spinal cord with surviving axons within descending long tracts, (*B*) spinal cord with reduced population of functional axons still present in the long, descending tracts.