THE CIRCUITRY OF THE HUMAN SPINAL CORD

Studies of human movement have proliferated in recent years, and there have been many studies of spinal pathways in humans, their role in movement, and their dysfunction in neurological disorders. This comprehensive reference surveys the literature related to the control of spinal cord circuits in human subjects, showing how they can be studied, their role in normal movement, and how they malfunction in disease states. The distinguished authors each bring to the book a lifetime's research and practice in neuroscience, motor control neurobiology, clinical neurology and rehabilitation. Chapters are highly illustrated and consistently organised, reviewing, for each pathway, the experimental background, methodology, organisation and control, role during motor tasks, and changes in patients with CNS lesions. Each chapter concludes with a helpful résumé that can be used independently of the main text to provide practical guidance for clinical studies. This is therefore the last word on the role of the spinal cord in human motor control. It will be essential reading for research workers and clinicians involved in the study, treatment and rehabilitation of movement disorders.

Emmanuel Pierrot-Deseilligny is Professor of Rehabilitation and Clinical Neurophysiology at the Hôpital de la Salpêtrière, University of Paris.

David Burke is Professor and Dean of Research and Development at the College of Health Sciences, University of Sydney.

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Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny
Hôpital de la Salpêtrière

and

David Burke
University of Sydney

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Contents

Preface

Spinal mechanisms in the control of movement. In the 1910–1920s Paul Hoffmann demonstrated that percutaneous electrical stimulation of the posterior tibial nerve in human subjects produced a synchronised response in the soleus muscle with the same central delay as the Achilles tendon jerk. This landmark study long preceded Lloyd's identification of the corresponding pathway in the cat (1943). Subsequently, much of the primary knowledge about the spinal circuitry has come from animal experiments, but human studies have retained a unique role: the ability to shed direct light on how spinal mechanisms are used in the control of voluntary movement. In the 1940–1950s, many spinal pathways were analysed in 'reduced' animal preparations with regard to their synaptic input and to their projections to other neurones.

Modern views about spinal pathways began to emerge when Anders Lundberg and colleagues showed in the 1960s and 1970s that, in the cat, each set of spinal interneurones receives extensive convergence from different primary afferents and descending tracts, and that the integrative function of spinal interneurones allows the motoneurones to receive a final command that has been updated at a premotoneuronal level. Methods have now been developed to enable indirect but nevertheless valid measurements of spinal interneuronal activity in human subjects, and these techniques have demonstrated reliability, particularly when congruent results are obtained with independent methods. Their use has allowed elucidation of how the brain modulates the activity of specific spinal

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Frontmatter
More information

interneurones to control movement. This, together with the abnormalities of motor control resulting from lesions in the central nervous system (CNS) and the underlying pathophysiology of movement disorders, is the subject of this book.

Over recent years, reappraisal of the role of direct cortico-motoneuronal projections in higher primates including humans has led to the view that the control of movement resides in the motor cortical centres that drive spinal motoneurone pools to produce the supraspinally crafted movement. This view belies the complex interneuronal machinery that resides in the spinal cord. It is a thesis of this book that the final movement is only that part of the supraspinally derived programme that the spinal cord circuitry deems appropriate. While the capacity of the spinal cord to generate or sustain even simple movements, particularly in human subjects, is limited, the influence that it plays in shaping the final motor output should not be underestimated. The recent recording by Eberhard Fetz and colleagues from spinal interneurones during, and before, voluntary movement in the awake monkey well illustrates this role of the spinal cord. A goal of rehabilitation of patients with upper motor neurone lesions should be to harness the residual motor capacities of the spinal cord and, for this to occur, the information in this book is critical. The techniques described in this book will also allow assessment in patients of whether any regeneration is 'appropriate'.

Studying motor control in human subjects. There has been an explosion of studies on human movement and of the dysfunction that accompanies different neurological disorders, and the prime rationale for this book is to summarise the literature related to the control of spinal cord circuitry in human subjects. Of necessity, only some interneuronal circuits can be studied reliably in human subjects, and no one book can provide a complete overview of the role of spinal circuitry in normal and pathological movement: there are no data for the many circuits that cannot yet be studied in human subjects, let alone the cat. This book is intended to provide a comprehensive account of (i) how some well-recognised and defined circuits can be studied, (ii) how they are used in normal movement, and (iii) how they malfunction in disease states.

It is as well to retain some reservations about conclusions of studies in human subjects: (i) All studies on human subjects are indirect and cannot be controlled as rigorously as in the cat. (ii) Some pathways cannot be explored quantitatively, because their effects are contaminated by effects due to other afferents (e.g. effects due to group II afferents are always contaminated by group I effects whatever testing method is used). (iii) For methodological reasons (stability of the stimulating and recording conditions), isometric voluntary contractions have been the main motor tasks during which changes in transmission in spinal pathways have been investigated. However, recent technological advances now allow the investigation of spinal pathways during natural movements, including reaching and walking. (iv) With transcranial magnetic stimulation of the motor cortex, it is possible to investigate the corticospinal control of spinal interneurones, but there are little data for other descending controls from basal ganglia and the brainstem, other than vestibular projections. (v) In patients, spinal circuitry has usually been explored under resting conditions, but the functionally important deficits may appear only during attempted movements (reinforcement of spasticity during movement, dystonia).

Methodological advances. The H reflex has served motor control well but, over the last 30 years, other techniques have been developed to allow more accurate probing of spinal pathways in human subjects, providing data that can validate and extend the findings from H reflex studies. As a result, knowledge of the role of spinal pathways in normal and pathological motor control has increased greatly, and this provides a further motivation for this book. For example, the use of *post-stimulus time histograms* has allowed the investigation of single motoneurones in human subjects, the technique of *spatial facilitation* allows the exploration of the convergence of different volleys on spinal interneurones, and *transcortical stimulation* of the motor cortex allows the corticospinal control of spinal pathways to be investigated. This book details this newer knowledge for the use of those who have an interest in the subject but who have not had time to read the rapidly accumulating original literature. Inevitably, there will be inconsistencies in conclusions from studies on intact human subjects who can respond to a stimulus. Greater validity comes from using a number of independent techniques to demonstrate the same finding, as is emphasised in the following chapters. Inconsistent or irreproducible findings can lead to controversy about the nature and the functional role of a specific pathway in normal subjects and in patients, and such inconsistencies are presented, and the validity of the method(s) used to explore that pathway is addressed. Possible future directions for the research are discussed.

Organisation of individual chapters. The different spinal pathways for which there are reliable and non-invasive methods of investigation are considered with, for each pathway:

(i) *A brief background from animal experiments.* Human investigations are indirect and it is crucial to know the essential characteristics of each pathway described in animal experiments with recordings from motoneurones and/or interneurones. Caution should always be taken in extrapolating from data obtained in 'reduced preparations' (anaesthetised, decerebrate or spinalised animals) to awake intact human subjects, but the validation of a technique for exploring a given pathway may require controls only possible in animal experiments and is more credible when there is a close analogy with animal experiments.

(ii) *A critical description of the available method(s)* that have been used to explore the relevant pathways selectively. Methodological details allowing the reader to use reliable methods are described.

(iii) *The organisation and descending control (in particular corticospinal) of these pathways in human subjects.* The basic organisation of each pathway may well be the same in humans and cats, but the strength of the projections of individual spinal pathways on different motoneurone pools and their descending control have been the subject of phylogenetic adaptations to different motor repertoires. For the human lower limb, more elaborate reflex assistance is required for bipedal stance and gait. That there has been this phylogenetic adaptation argues that spinal pathways have a functional role in human subjects and are not evolutionary relics.

(iv) *The changes in transmission in these pathways during various motor tasks.* How spinal reflex pathways are used in motor control cannot be deduced from experiments on 'reduced' animal preparations. It requires experiments performed during natural movements, as can be done in humans. This has been one major contribution of human studies to the understanding of motor control physiology. Thus, even though many of the conclusions are speculative, this book gives a large place to the probable functional implications of the described changes in transmission in spinal pathways during movement.

(v) *Changes in transmission in these pathways in patients with various lesions of the CNS.* This has provided new insights about the pathophysiology of the movement disorder in these patients.

Overall organisation of the book. The general methodologies that are used for investigating pathways are considered in a first chapter with, for each method, its advantages and its disadvantages. There is a risk that starting with a technical chapter would dissuade the non-specialist reader from delving further into the book. This *initial chapter* is useful to understand fully the particular techniques used for the investigation of the different pathways, *but it is not essential for comprehension of the following chapters.*

For those who wish to know how methods and concepts have evolved over the years and why some interpretations were erroneous even if, at the time, influential, the methods are described in detail, with their limits and caveats, and the results obtained and their interpretation(s) are critically evaluated in each chapter. Because human studies are fraught with technical difficulties, much space has been alloted to methods and potential pitfalls.

For those who want to get to the gist of the matter reasonably quickly each chapter terminates with a résumé of its salient points. The résumés can be used on their own without reference to the detailed text. They give a practical 'recipe' on the choice of the appropriate technique and its proper use in routine clinical studies, together with data on the possible functional role of the particular pathway in motor control and in the pathophysiology of movement disorders.

The final two chapters summarise and synthesise the changes in transmission in spinal pathways during movement and how these changes contribute to motor control, and spinal mechanisms underlying spasticity and motor impairment in patients with Parkinson's disease. In these chapters, the physiological (Chapter 11) and pathophysiological (Chapter 12) roles of different spinal pathways, considered in the previous chapters, are presented with another approach: (i) how different motor tasks are controlled by spinal pathways (Chapter 11); (ii) how these pathways contribute to motor disorders (Chapter 12).

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Abbreviations

5-HT	5-hydroxytryptophan
ACh	acetylcholine
Aff.	affected
AHP	afterhyperpolarisation
APB	abductor pollicis brevis
Bi	biceps
CFS	critical firing stimulus
Co FRA	contralateral FRA
CPN	common peroneal nerve
CS or (Cort. sp.)	corticospinal
CUSUM	cumulative sum
Cut	cutaneous
Desc.	descending
DPN	deep peroneal nerve
ECR	extensor carpi radialis
ED	extensor digitorum
EDB	extensor digitorum brevis
EDL	extensor digitorum longus
EHB	extensor hallucis brevis
EHL	extensor hallucis longus
EMG	electromyogram
EPSP	excitatory post-synaptic potential
Erect sp	erector spinae
Exc	excitatory
FCR	flexor carpi radialis
FCU	flexor carpi ulnaris
FDB	flexor digitorum brevis
FDI	first dorsal interosseus
FDS	flexor digitorum superficialis
FHB	flexor hallucis brevis
FN	femoral nerve
FPL	flexor pollicis longus

FRA	flexion reflex afferent
Glut Max (or Glut)	gluteus maximus
GM	gastrocnemius medialis
GS	gastrocnemius-soleus
GTO	Golgi tendon organ
H	hamstrings
IN	interneurone
Inhib.	inhibitory
IPSP	inhibitory post-synaptic potential
ISI	inter-stimulus interval
L-Ac	L-acetylcarnitine
LC (or Loc. coer).	locus coeruleus
MC	musculo-cutaneous
MEP	motor evoked potential
MLR	medium-latency response
MN	motoneurone
MRI	magnetic resonance imaging
MT	motor threshold
MVC	maximal voluntary contraction
NA	noradrenaline
NRM	nucleus raphe magnus
PAD	primary afferent depolarisation
Per Brev	peroneus brevis
PL	peroneus longus
PN	propriospinal neurone
Ps	psoas
PSP	post-synaptic potential
PT	perception threshold
PTN	posterior tibial nerve
Q	quadriceps
RC	Renshaw cell
Rect Abd	rectus abdominis
RS or (Ret. Sp).	reticulo-spinal
Rubr. sp.	rubro-spinal
SLR	short-latency response
Sol	soleus
SPN	superficial peroneal nerve
SSEP	somatosensory evoked potential
Stim.	stimulus
TA	tibialis anterior
TFL	tensor fasciae latae
TMS	trans cranial magnetic stimulation
TN	tibial nerve
Tri	triceps brachii
Unaff.	unaffected
VI	vastus intermedius
VL	vastus lateralis
VS	vestibulo-spinal