THE CIRCUITRY OF THE HUMAN SPINAL CORD: SPINAL AND CORTICOSPINAL MECHANISMS OF MOVEMENT

Studies of human movement have proliferated in recent years. This greatly expanded and thoroughly updated reference surveys the literature on the corticospinal control of spinal cord circuits in human subjects, showing how different circuits can be studied, their role in normal movement and how they malfunction in disease states. 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 central nervous system lesions. Each chapter concludes with a helpful résumé that can be used independently of the main text to provide practical guidance for clinical studies. The final four chapters bring together the changes in transmission in spinal and corticospinal pathways during movement and how they contribute to the desired movement. This book is essential reading for research workers and clinicians involved in the study, treatment and rehabilitation of movement disorders.

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Spinal and Corticospinal Mechanisms of Movement

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Preface

This book is the direct descendant of our book entitled *The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders*, published in 2005 by Cambridge University Press. A revised and updated edition was needed because in 7 years new and more recent data have changed views about the role of the spinal cord in the control of limb movement. This revised edition also takes into account the development and rapid uptake of investigations using transcranial stimulation of the motor cortex. Thus, much more attention has been put on the corticospinal control of movement and transcortical pathways. Neural plasticity, whether underlying learning a new skill by healthy subjects or compensatory mechanisms for the neural changes associated with ageing or disease, has also been the subject of many recent investigations that deserve to be considered.

The book is dedicated to Anders Lundberg (1920–2009). Anders Lundberg is rightfully seen as the father of modern spinal cord neurophysiology, on how spinal circuitry is mobilised by descending commands and how feedback modifies the command at spinal cord level. Anders Lundberg was an outstanding leader, an intense and focused researcher, a tough critic, a good listener and inspiring mentor. He and his students provided much of the background data from animal experiments for the human studies which this book attempts to summarise. Above all, not only did he lead the world in the definition of interneuronal mechanisms in the spinal cord but he also developed hypotheses about how these mechanisms would be used in the intact organism. In later years, having defined the C3–C4 propriospinal system in the cat, he undertook behavioural experiments to confirm its role

in movement, and it remains the only carefully documented interneuronal system for which a functional purpose has been clearly identified. His enthusiasm and enormous intellect have provided an impetus for us to show how discoveries from animal experiments have benefited the human condition, despite the adaptations that are necessary to cater for the greater motor repertoire of human subjects.

In the preface to our previous book, we wrote: *Over recent years, reappraisal of the role of direct corticomotoneuronal 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.* This statement remains, we believe, as true today as it was in 2005 and it is also a driving motivation behind this volume. As research interest shifts to the complexities of the cortical mechanisms in the control of movement, so too has the thrust of this new book shifted to encompass transcortical reflexes, motor cortex excitability and corticospinal mechanisms in greater detail. Nevertheless, it is timely to remind the reader that limb movements can be planned and their programs initiated by the brain but they cannot be performed without a spinal cord and they cannot be performed gracefully without the intricate feedback systems that reside within it.

As mentioned above, there has been an explosion of literature on motor control over the past 7 years, much of it devoted to cortical mechanisms preceding and associated with movement, and even some that do not have any direct influence on spinal circuitry. However, even in the latter instance, the state of the spinal cord is important when the procedures involved in testing the cortical circuitry depend on the modulation of a response that is transmitted through spinal mechanisms. In reviewing the literature for this book, we have become concerned that so simple a fact has been so often ignored in publications, even in prestigious journals.

However, the justification for a new book ultimately resides not in restating the obvious but in whether there is anything new to say, and accordingly it should be asked, *precisely what is new in this book?*

- To understand the influence of cortical mechanisms on the spinal motoneurone pools it is necessary to understand, first, how segmental mechanisms can modulate the command signal and, second, the limitations of techniques that can be used in human subjects to demonstrate appropriate changes. Accordingly, the structure of the initial chapters in this new book recapitulates that of the previous book – but each has been updated to cover new findings, new techniques and new appreciations of advantages and disadvantages.
- In a new chapter, the largest in this volume, we focus more fully on the techniques (and their limitations) used to study cortical and corticospinal mechanisms in the control of movement and on the results of such studies. It thereby provides an overview that integrates spinal and cortical mechanisms so that those who work at one end of the neuraxis can appreciate the importance of the other.
- A further major advance over the last decade has been on the plastic changes in connectivity that occur with development, senescence, motor learning, disease and recovery from it. An understanding of how the nervous system can adapt to changed circumstances is the key to understanding, on the one hand, acquired differences in motor skill and, on the other hand, the compensations, sometimes dysfunctional, that occur when the nervous system is damaged. Accordingly appropriate data are highlighted in chapters focussed on specific circuits, and there is a new chapter that specifically addresses the short- and long-standing adaptations of the function of spinal and corticospinal circuits to altered demands and pathology.

Organisation of Individual Chapters

We have retained the same format as for the previous book, with consideration first of the different spinal pathways for which there are reliable and non-invasive

methods of investigation. Accordingly, after an extensive chapter on Methodology, we consider spinal circuitry in Chapters 2–10 with, for each circuit:

1. *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 the results in human subjects are more credible when there is a close analogy with animal experiments.
2. *A critical description of the available method(s)* that have been used to explore the relevant pathways selectively. 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 allotted to methods and potential pitfalls.
3. *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.
4. *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.
5. *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

We have again adopted much the same organisation as previously.

Methodology. The general methodologies which are used for investigating pathways are considered in a first chapter with the advantages and disadvantages of each technique. There is a risk that starting with a technical chapter would dissuade the non-specialist reader from delving further into the book. However, this initial chapter is useful to understand the rationale, advantages and limitations of the different techniques used to investigate different pathways, and we consider it important for those who have no experience with a particular technique but wish to use it in human subjects. Nevertheless it is not essential for the comprehension of subsequent chapters.

Résumés. 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.

Overviews. The final four chapters summarise and synthesise the changes in transmission in spinal and corticospinal 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 and dystonia. The physiological and pathophysiological roles of spinal and corticospinal pathways are presented using a different approach to that in the previous chapters. With respect to the previous book, these overviews have been greatly developed.

A long chapter (Chapter 11) is focussed on purposeful movements and involves:

(i) an overview of the contribution made by the different spinal pathways in various kinds of movement,
(ii) an attempt to unravel the relationships between volitional control, afferent feedback (in particular through transcortical reflexes), and possible efference copy,
(iii) a description of the changes in motor cortex excitability and short interval intracortical inhibition (SICI) during the different phases of various movement, and
(iv) the role of spinal and supraspinal factors in muscle fatigue.

Chapter 12 considers the contribution of spinal and transcortical pathways in unperturbed and perturbed stance and gait.

Plastic changes in spinal and corticospinal circuits are considered in Chapter 13.

In a brief summary, Chapter 14 collates data in preceding chapters on spinal mechanisms underlying spasticity and the motor impairment in patients with Parkinson's disease and dystonia.

Abbreviations

Ach	acetylcholine
ACT	afferent conduction time
ADM	abductor digiti minimi
AG1	first agonist burst
AG2	second agonist burst
AHP	afterhyperpolarisation
ALS	amyotrophic lateral sclerosis
ANT	antagonist burst
APB	abductor pollicis brevis
APL	abductor pollicis longus
BB	biceps brachii
BF	biceps femoris
BR	brachioradialis
CMEP	cervicomedullary motor evoked potential
CNS	central nervous system
CoM	centre of mass
CPG	central pattern generator
CPN	common peroneal nerve
CS	corticospinal tract
CSP	contralateral silent period
CSP	cutaneous silent period
CT	conduction time
CUSUM	cumulative sum
CV	conduction velocity
D-wave	direct wave of the corticospinal volley
DPN	deep peroneal nerve
E1	early cutaneomuscular excitation
E2	late cutaneomuscular excitation
ECR	extensor carpi radialis
ECT	efferent conduction time
ECU	extensor carpi ulnaris
ED	extensor digitorum

EDB	extensor digitorum brevis
EDL	extensor digitorum longus
EEG	electroencephalogram
EHB	extensor hallucis brevis
EHL	extensor hallucis longus
EMG	electromyogram
EPSP	excitatory post-synaptic potential
FA	fractional anisotropy
FCR	flexor carpi radialis
FCU	flexor carpi ulnaris
FDB	flexor digitorum brevis
FDI	first dorsal interosseous
FDP	flexor digitorum profundus
FDS	flexor digitorum superficialis
FHB	flexor hallucis brevis
fMRI	functional magnetic resonance imaging
FN	femoral nerve
FPL	flexor pollicis longus
FRA	flexion reflex afferents
GABA	gamma-aminobutyric acid
GL	gastrocnemius lateralis
GM	gastrocnemius medialis
GS	gastrocnemius–soleus
GTO	Golgi tendon organ
H'	test reflex, paired H reflex technique for recurrent inhibition
H1	conditioning H reflex, paired H reflex technique for recurrent inhibition
HD	homosynaptic depression
H_{max}	maximal H reflex
I-wave	indirect wave of the corticospinal volley
I1	cutaneomuscular inhibition
Ia IN	Ia inhibitory interneurone
Ib IN	Ib interneurone
ICF	intracortical facilitation
IHI	interhemispheric inhibition
IN	interneurone
IPSP	inhibitory post-synaptic potential
ISI	interstimulus interval
iSP	ipsilateral cortical silent period
L-Ac	L-acetylcarnitine
LAI	long-latency afferent inhibition
LICF	long-interval intracortical facilitation
LICI	long-interval intracortical inhibition
LL response	long-latency response
LLSR	long-latency stretch reflex
Loc Coer	locus coeruleus
LRN	lateral reticular nucleus
LTD	long-term depression
LTI	linear-time-invariant
LTP	long-term potentiation
M wave	direct motor response
M1	primary motor cortex
M1	short-latency stretch response
M2	long-latency stretch response (upper limb)
M2	medium-latency stretch response (lower limb)
M3	long-latency stretch response
MC	musculo-cutaneous
MEP	motor evoked potential
MLSR	medium-latency stretch response
M_{max}	maximal direct motor response
MN	motoneurone
MS	multiple sclerosis
MT	motor threshold
MU	motor unit
MVC	maximal voluntary contraction
NA	noradrenergic
NRM	nucleus raphe magnus
PAD	primary afferent depolarisation
PAD IN	interneurone mediating primary afferent depolarisation
PAS	paired associative stimulation
PB	peroneus brevis
PD	posterior deltoid
PET	positron emission tomography
PIC	persistent inward current
PL	peroneus longus
PM	pectoralis major
PN	propriospinal neurone
PSF	post-stimulus frequencygram
PSP	post-synaptic potential
PSTH	post-stimulus time histogram
PT	perception threshold
PTN	posterior tibial nerve
PTP	post-tetanic potentiation
RC	Renshaw cell

REM	rapid eye movements
RF	rectus femoris
rTMS	repetitive TMS
S1	conditioning stimulus, paired H reflex technique for recurrent inhibition
SAI	short-latency afferent inhibition
SCI	spinal cord injury
SD	standard deviation
SEM	standard error of the mean
SICF	short-interval intracortical facilitation
SICI	short-interval intracortical inhibition
SLSR	short-latency stretch reflex
SM	test stimulus, paired H reflex technique for recurrent inhibition
SPN	superficial peroneal nerve
SR	superficial radial
SSEP	somatosensory evoked potential
ST	semitendinosus
TA	tibialis anterior
TBS	theta burst stimulation
tDCS	transcranial direct current stimulation
TENS	transcutaneous electrical nerve stimulation
TES	transcranial electrical stimulation
TFL	tensor fascia latae
TMS	transcranial magnetic stimulation
TN	tibial nerve
Tri	triceps brachii
TT	tendon jerk threshold
TVR	tonic vibration reflex
UMN	upper motoneurone
V1	reflex response following M_{max} during voluntary contraction
VL	vastus lateralis
VM	vastus medialis
VS	vestibulospinal tract
VSCT	ventral spinocerebellar tract