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0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

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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.

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Its Role in Motor Control
and Movement Disorders

Emmanuel Pierrot-Deseilligny

Hôpital de la Salpêtrière

and

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Contents

Preface	<i>page</i> xv
Acknowledgements	xix
List of abbreviations	xxi
1 General methodology	1
The monosynaptic reflex : H reflex and tendon jerk	1
Initial studies	1
Underlying principles	2
Basic methodology	4
Limitations related to mechanisms acting on the afferent volley of the reflex	11
‘Pool problems’ related to the input–output relationship in the motoneurone pool	16
Normative data and clinical value	20
Critique: limitations, advantages and conclusions	21
The F wave	21
Underlying principles and basic methodology	21
Characteristics of the F wave	22
F wave as a measure of excitability of motoneurones	23
Clinical applications	24
Conclusions	24
Modulation of the on-going EMG activity	24
Underlying principles and basic methodology	24
Changes in the on-going EMG and in the H reflex need not be identical	26

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)

vi Contents

Post-stimulus time histograms (PSTHs)		Stimulation of the motor cortex	55
of the discharge of single motor units	28	Spatial facilitation	56
Underlying principles	29	Coherence analysis in EMG/EMG or	
Basic methodology	29	EEG/EMG signals	56
Assessment of the timing of the		References	56
changes in firing probability	32		
Assessment of the size and significance		2 Monosynaptic Ia excitation and	
of the peaks and troughs in the PSTH	34	post-activation depression	63
Critique: limitations, advantages and		Background from animal experiments	64
conclusions	36	Initial findings	64
Unitary H reflex	37	Pathway of monosynaptic Ia excitation	64
Underlying principles and basic		Distribution of heteronymous	
methodology	37	monosynaptic Ia excitation	65
Significance of changes in CFS		The stretch reflex	66
produced by conditioning stimuli	38	Methodology	66
Critique: limitations, advantages and		Underlying principles	66
conclusions	39	Homonymous monosynaptic Ia	
Stimulation of the motor cortex	39	excitation	66
EMG responses evoked by cortical		Heteronymous monosynaptic Ia	
stimulation	39	excitation	70
Electrical stimulation	40	Range of electrical thresholds of Ia	
Magnetic stimulation	42	afferents when stimulating using	
Critique: advantages, limitations,		surface electrodes	77
conclusions	44	Organisation and pattern of connections	79
Spatial facilitation	45	Homonymous monosynaptic Ia	
Underlying principles	45	excitation	79
Spatial facilitation judged in the PSTH		Heteronymous monosynaptic Ia	
of single units recordings	46	excitation in the lower limb	81
Spatial facilitation judged from		Heteronymous monosynaptic Ia	
monosynaptic test reflexes	47	excitation in the upper limb	83
Conclusions	48	Developmental changes in	
Coherence analysis between EMG/EMG		heteronymous Ia connections	86
or EEG/EMG signals	48	Motor tasks and physiological	
Cross-correlation	48	implications	87
Coherence techniques	48	Homonymous monosynaptic Ia	
General conclusions	49	excitation. Stretch reflex	
Methods	49	responses	87
Development	49	Heteronymous monosynaptic Ia	
Résumé	49	excitation	92
Monosynaptic reflex	49	Studies in patients and clinical	
F wave	52	implications	95
Modulation of the on-going EMG	53	Methodology	95
Post-stimulus time histograms		Peripheral neuropathies,	
(PSTHs) of the discharge of single		mononeuropathies and proximal	
motor units	53	nerve lesions	95
Unitary H reflex	54	Spasticity	96

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)

	Contents	vii
Post-activation depression at the Ia afferent-motoneurone synapse	96	
Background from animal experiments	96	
Functional significance	97	
Methodology	97	
Post-activation depression in spastic patients	99	
Conclusions	100	
Role of monosynaptic Ia excitation in natural motor tasks	100	
Changes in monosynaptic Ia excitation in patients	101	
Résumé	101	
Importance of studies of Ia connections	101	
Background from animal experiments	101	
Methodology	102	
Organisation and pattern of connections	103	
Motor tasks and physiological implications	104	
Studies in patients and clinical implications	105	
Post-activation depression at the Ia-motoneurone synapse	106	
References	106	
3 Muscle spindles and fusimotor drive: microneurography and other techniques	113	
Background from animal experiments	113	
Initial investigations	113	
Current views of spindle structure and function	114	
β (skeletal-fusimotor) neurones	117	
Methodology	117	
Discredited techniques	117	
Acceptable techniques	119	
Critique of the tests to study muscle spindle afferent discharge and fusimotor drive	126	
Organisation and pattern of connections	127	
Background fusimotor drive	127	
Effects of cutaneous afferents on fusimotor neurones	127	
Corticospinal volleys	130	
Effects of muscle vibration on human muscle spindles	130	
Motor tasks and physiological implications	131	
Reflex reinforcement by remote muscle contraction: the Jendrassik manoeuvre	131	
Effects of voluntary effort on fusimotor drive to the contracting muscle	133	
Possible role of the fusimotor system during normal movement	136	
Studies in patients and clinical implications	138	
Spasticity	139	
Parkinson's disease	140	
Conclusions	141	
Résumé	142	
Background from animal experiments	142	
Methodology	142	
Critique of the tests to study fusimotor drive	143	
Organisation and pattern of connections	143	
Motor tasks and physiological implications	144	
Changes in fusimotor activity in patients	145	
References	145	
4 Recurrent inhibition	151	
Background from animal experiments	151	
Initial findings	151	
General features	151	
Input to Renshaw cells	152	
Projections of Renshaw cells	153	
Conclusions	154	
Methodology	154	
Using homonymous antidromic motor volleys is an invalid technique in humans	154	
The paired H reflex technique to investigate homonymous recurrent inhibition	155	
Methods for investigating heteronymous recurrent inhibition	161	

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)**viii Contents**

Organisation and pattern of connections	169	5 Reciprocal Ia inhibition	197
Homonymous recurrent projections to motoneurones	169	Background from animal experiments	197
Heteronymous recurrent projections to motoneurones in the lower limb	169	Initial findings	197
Heteronymous recurrent projections to motoneurones in the upper limb	170	General features	198
Recurrent inhibition of interneurones mediating reciprocal Ia inhibition	171	Projections from Ia interneurones	199
Corticospinal suppression of recurrent inhibition	173	Input to Ia interneurones	199
Motor tasks and physiological implications	173	Presynaptic inhibition	200
Recurrent inhibition of motoneurones of a muscle involved in selective contractions	173	Conclusions	201
Recurrent inhibition during contraction of the antagonistic muscle	180	Methodology	201
Recurrent inhibition of antagonistic muscles involved in co-contraction	180	Underlying principles	201
Heteronymous recurrent inhibition and heteronymous Ia excitation	183	Inhibition of various responses	201
Studies in patients and clinical implications	184	Evidence for reciprocal Ia inhibition	204
Spasticity	184	Critique of the tests to study reciprocal Ia inhibition	208
Patients with other movement disorders	187	Organisation and pattern of connections	209
Conclusions	187	Pattern and strength of reciprocal Ia inhibition at rest at hinge joints	209
Changes in recurrent inhibition in normal motor control	187	Absence of 'true' reciprocal Ia inhibition at wrist level	211
Changes in recurrent inhibition and pathophysiology of movement disorders	188	Cutaneous facilitation of reciprocal Ia inhibition	214
Résumé	188	Descending facilitation of reciprocal Ia inhibition	215
Background from animal experiments	188	Motor tasks and physiological implications	217
Methodology	188	Voluntary contraction of the antagonistic muscle	217
Organisation and pattern of connections	190	Reciprocal Ia inhibition directed to motoneurones of the active muscle	223
Motor tasks and physiological implications	191	Reciprocal Ia inhibition during co-contraction of antagonistic muscles	225
Studies in patients and clinical implications	192	Changes in reciprocal Ia inhibition during postural activity	227
References	192	Changes in reciprocal Ia inhibition during gait	227
		Studies in patients and clinical implications	229
		Methodology	229
		Spasticity	229
		Patients with cerebral palsy	233
		Patients with hyperekplexia	233
		Patients with Parkinson's disease	233
		Changes in non-reciprocal group I inhibition at wrist level	234

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)

	Contents	ix
Conclusions	234	
Role of reciprocal Ia inhibition in motor tasks	234	
Changes in reciprocal Ia inhibition and pathophysiology of movement disorders	235	
Résumé	235	
Background from animal experiments	235	
Methodology	235	
Organisation and pattern of connections	236	
Motor tasks and physiological implications	237	
Studies in patients and clinical implications	238	
References	239	
6 Ib pathways	244	
Background from animal experiments	244	
Initial findings	244	
Golgi tendon organs and Ib afferents	245	
General features	245	
Projections of Ib afferents	246	
Input to Ib interneurons	247	
Contraction-induced Ib inhibition	248	
Presynaptic inhibition and post-activation depression	248	
Reflex reversal during fictive locomotion	248	
Methodology	249	
Ib inhibition	249	
Evidence for Ib inhibition	252	
Oligosynaptic group I excitation	255	
Critique of the tests to reveal Ib effects	255	
Organisation and pattern of connections	256	
Pattern and strength of Ib inhibition	256	
Oligosynaptic group I excitation	258	
Convergence of Ia afferents onto interneurons mediating Ib inhibition	260	
Effects of low-threshold cutaneous afferents	261	
Facilitation of Ib inhibition by joint afferents	263	
Effects from nociceptive afferents	265	
Descending effects	265	
Multiple convergence onto common interneurons	265	
Conclusions: necessity for convergence of multiple inputs	267	
Motor tasks and physiological implications	267	
Suppression of Ib inhibition to voluntarily activated motoneurons	268	
Ib inhibition directed to motoneurons not involved in the voluntary contraction	272	
Changes in Ib inhibition during walking	273	
Studies in patients and clinical implications	275	
Ib inhibition	275	
Ib excitation in spastic patients	277	
Conclusions	279	
Role of changes in Ib inhibition during motor tasks	279	
Changes in Ib pathways and the pathophysiology of movement disorders	279	
Résumé	279	
Background from animal experiments	279	
Methodology	280	
Organisation and pattern of connections	280	
Motor tasks and physiological implications	281	
Studies in patients and clinical implications	282	
References	283	
7 Group II pathways	288	
Background from animal experiments	288	
Initial findings	288	
Muscle spindle secondary endings and group II afferents	289	
Synaptic linkage	289	
Projections from group II interneurons	291	

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)**x Contents**

Excitatory inputs to group II interneurons	291	Organisation and pattern of connections	330
Inhibitory control systems	292	Motor tasks and physiological implications	331
Methodology	293	Studies in patients and clinical implications	331
Underlying principles	293	References	332
Stretch-induced homonymous group II excitation of leg and foot muscles	293	8 Presynaptic inhibition of Ia terminals	337
Electrically induced heteronymous group II excitation	293	Background from animal experiments	337
Evidence for muscle group II excitation	297	Initial findings	337
Critique of the tests used to reveal group II actions	299	General features	337
Organisation and pattern of connections	302	Inputs to PAD interneurons	339
Peripheral pathway	302	Selectivity of the control of presynaptic inhibition	339
Central pathway of group II excitation	303	Conclusions	340
Distribution of group II excitation	304	Methodology	340
Convergence with other peripheral afferents	305	Discrepancy between the variations in the on-going EMG and those in the H reflex	340
Peripheral inhibitory input to interneurons co-activated by group I and II afferents	307	Activating PAD INs by a conditioning volley to assess their excitability	340
Corticospinal control of peripheral facilitation	307	Background presynaptic inhibition inferred from Ia facilitation of the H reflex	345
Motor tasks and physiological implications	310	Techniques using single motor units	346
Voluntary contractions	310	Conclusions	347
Postural tasks	312	Organisation and pattern of connections	347
Changes in group II excitation during gait	314	Projections on Ia terminals directed to different motoneurone types	347
Studies in patients and clinical implications	320	Organisation in subsets with regard to the target motoneurons of Ia afferents	348
Peripheral neuropathies	320	Peripheral projections to PAD interneurons	348
Spasticity	320	Corticospinal projections	350
Parkinson's disease	326	Vestibulospinal projections	353
Conclusions	326	Tonic level of presynaptic inhibition of Ia terminals	353
Role of group II pathways in natural motor tasks	326	Weak sensitivity of stretch-evoked Ia volleys to presynaptic inhibition	354
Changes in group II excitation and pathophysiology of movement disorders	328	Motor tasks and physiological implications	355
Résumé	328		
Background from animal experiments	328		
Methodology	328		

	Contents	xi
Ia terminals on lower limb		
motoneurons involved in voluntary contractions	355	
Ia terminals directed to motoneurons of inactive synergistic muscles	359	
Presynaptic inhibition of Ia terminals during contraction of antagonistic muscles	360	
Presynaptic inhibition of Ia terminals during contraction of remote muscles	361	
Changes in presynaptic inhibition of Ia terminals on upper limb motoneurons	362	
Changes in presynaptic inhibition during upright stance	363	
Changes in presynaptic inhibition during gait	365	
Studies in patients and clinical implications	367	
Methodology	367	
Spasticity	368	
Changes in presynaptic inhibition in Parkinson's disease	371	
Changes in presynaptic inhibition of Ia terminals in patients with dystonia	371	
Conclusions	372	
Role of changes in presynaptic inhibition of Ia terminals in normal motor control	372	
Changes in presynaptic inhibition and pathophysiology of movement disorders	373	
Résumé	373	
Background from animal experiments	373	
Methodology	374	
Organisation and pattern of connections	375	
Motor tasks and physiological implications	376	
Studies in patients and clinical implications	377	
References	378	
9 Cutaneomuscular, withdrawal and flexor reflex afferent responses	384	
Background from animal experiments	385	
Initial findings	385	
Cutaneous responses mediated through 'private' pathways	385	
FRA reflex pathways	388	
Conclusions	391	
Methodology	391	
Underlying principles	391	
Stimuli	391	
Responses recorded at rest	394	
Modulation of motoneurone excitability	396	
Critique of the tests to study cutaneous effects	396	
Organisation, connections and physiological implications of withdrawal reflexes	399	
Afferent pathway of withdrawal reflexes	399	
Central pathway of early withdrawal responses	400	
Functional organisation of early withdrawal reflexes	401	
Late withdrawal responses	407	
Interactions between different inputs in withdrawal reflex pathways	411	
Changes in withdrawal reflexes during motor tasks	412	
Organisation, connections and physiological implications of cutaneomuscular reflexes evoked by non-noxious stimuli	414	
The different responses	414	
Afferent conduction	418	
Central pathway of short-latency responses occurring at 'spinal latency'	418	
Central pathway for long-latency effects	421	
Projections of cutaneous afferents to different types of motoneurons	424	

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)**xii Contents**

Pattern and functional role of early responses	427	Inhibition of propriospinal neurones via feedback inhibitory interneurons	463
Changes in patients and clinical implications	432	Interaction between excitatory and inhibitory inputs	467
Complete spinal transection	433	Organisation of the cervical propriospinal system	468
Upper motoneurone lesions other than those due to a complete spinal transection	433	Motor tasks and physiological implications	471
Grasp reflex	436	Evidence for propriospinal transmission of a part of the descending command	471
Parkinson's disease	436	Propriospinally mediated facilitation of motoneurons during voluntary contraction	474
Peripheral neuropathies	437	Functional implications: role of the propriospinal relay in normal motor control	476
Diagnostic uses	437	Studies in patients and clinical implications	479
Conclusions	438	Patient with a discrete lesion of the spinal cord at the junction C6–C7 spinal level	479
Role of cutaneous reflexes in motor control	438	Stroke patients	481
Changes in cutaneous reflexes in patients	438	Patients with Parkinson's disease	484
Résumé	439	Conclusions	485
Background from animal experiments	439	Role of propriospinal transmission of a part of the descending command	485
Methodology	440	Changes in propriospinal transmission of the command in patients	485
Withdrawal reflexes	441	Résumé	486
Cutaneomuscular reflexes evoked by non-noxious stimuli	442	Background from animal experiments	486
Studies in patients and clinical implications	444	Methodology	486
References	445	Organisation and pattern of connections	487
10 Propriospinal relay for descending motor commands	452	Motor tasks and physiological implications	488
The cervical propriospinal system	452	Studies in patients and clinical implications	489
Background from animal experiments	452	The lumbar propriospinal system	490
The propriospinal system in the cat	452	Background from animal experiments	490
Conflicting results in the monkey	454	Methodology	491
Methodology	455	Underlying principle	491
Propriospinally mediated excitation produced by peripheral volleys	455		
Cutaneous suppression of descending excitation	458		
Rostral location of the relevant interneurons with respect to motoneurons	459		
Organisation and pattern of connections	460		
Excitatory inputs to propriospinal neurones	460		

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)

	Contents	xiii
Non-monosynaptic excitation of voluntarily activated single motor units	491	Cutaneomuscular responses 514 Suppression of transmission in inhibitory pathways 514 Conclusions 515
Non-monosynaptic excitation of compound EMG responses	493	Flexion–extension movements involving hinge joints 515
Rostral location of the relevant interneurons	493	Afferent discharges accompanying a voluntary flexion–extension movement 515
Organisation and pattern of connections	494	Excitation of active motoneurons 516
Peripheral excitatory input to excitatory lumbar propriospinal neurones	494	Control of different features of the movement 517
Peripheral inhibitory inputs to lumbar propriospinal neurones	496	Recruitment of different types of motor units 518
Peripheral inhibition of motoneurons	497	Inhibition of antagonists 519
Corticospinal control	498	Timing of the different effects 520
Motor tasks and physiological implications	500	Different strategies for proximal and distal movements 521
Propriospinally mediated changes in the quadriceps H reflex during weak contractions	500	Conclusions 522
Modulation of the on-going EMG during different motor tasks	502	Movements involving ball joints 522
Functional implications	502	Different organisation of the human spinal circuitry at wrist level 522
Studies in patients and clinical implications	503	Non-reciprocal group I inhibition during wrist movements 524
Spasticity	503	Changes in presynaptic inhibition on Ia terminals on wrist motoneurons 526
Patients with Parkinson's disease	503	Other spinal pathways possibly involved in wrist movements 526
Conclusions	505	Co-ordinated activation of various synergies 527
Résumé	505	Where are motor synergies laid down? 527
Background from animal experiments	505	Synergies based on 'hardwired' spinal connections 528
Methodology	505	Cervical propriospinal system 529
Organisation and pattern of connections	505	State-dependent modulation of sensory feedback 530
Motor tasks and physiological implications	506	Motor learning 530
Studies in patients and clinical implications	506	Co-contractions of antagonists at the same joint 531
References	506	Control of spinal pathways during co-contraction of antagonists 531
11 Involvement of spinal pathways in different motor tasks	511	Control of the decreased inhibition between antagonists 533
Isometric tonic contractions	512	
Fusimotor drive	512	

xiv Contents

Joint stiffness	533	Possible spinal mechanisms underlying the pathophysiology of spasticity at rest	560
Control of the stretch reflex at hinge joints	534	Why do spinal pathways malfunction?	571
Control of the excitation at ball joints	534	Changes in the intrinsic properties of muscles fibres (contracture)	572
Conclusions	535	Changes in spinal pathways during movements in spasticity	573
Maintenance of bipedal stance	535	Pathophysiology of spasticity after cerebral lesions	575
Normal quiet standing	535	Pathophysiology of spasticity after spinal lesions	580
Unstable postural tasks requiring prolonged muscle contractions	537	Conclusions	582
Responses to fast transient perturbations of stance	538	Parkinson's disease	582
Gait	542	Possible mechanisms underlying Parkinsonian rigidity	582
Characteristics of human walking	542	Transmission in spinal pathways at rest	584
Changes in transmission in spinal pathways during normal walking	545	Alterations of transmission in spinal pathways during motor tasks	589
Reactions to external perturbations	547	Conclusions	592
Running, hopping, landing	550	References	592
References	550	Index	601
12 The pathophysiology of spasticity and parkinsonian rigidity	556		
Spasticity	556		
What is spasticity? What is it not?	557		
Spasticity and animal decerebrate rigidity are unrelated	560		

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)

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

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)

xvi Preface

interneurons 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 interneurons 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 stud-

ied, (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 interneurons, 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 motoneurons in human subjects, the technique of *spatial facilitation* allows the exploration of the convergence of different volleys on spinal interneurons, 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

Cambridge University Press

0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

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Frontmatter

[More information](#)

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 motoneurons and/or interneurons. 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 motoneuron 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

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0521825814 - The Circuitry of the Human Spinal Cord: Its Role in Motor Control and Movement Disorders

Emmanuel Pierrot-Deseilligny and David Burke

Frontmatter

[More information](#)

xviii Preface

technical difficulties, much space has been allotted 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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Frontmatter

[More information](#)

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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

xxii **List of abbreviations**

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