The Integrative Action of the Autonomic Nervous System

Almost all bodily functions are dependent on activity of the autonomic nervous system - from the cardiovascular system, the gastrointestinal tract, the evacuative and sexual organs, to the regulation of temperature, metabolism and tissue defense. Balanced functioning of each aspect of this system is an important basis of our life and wellbeing. In this long-awaited second edition, the author, a leading figure in this field, provides an up-to-date and detailed description of the cellular and integrative organization of the autonomic nervous system, covering both peripheral and central aspects. The book exposes modern neurobiological concepts that allow us to understand why this system normally runs so smoothly and why its deterioration has such disastrous consequences. This broad overview will appeal to researchers and advanced undergraduate students of the various biological and medical sciences studying how the autonomic nervous system

works and to clinicians and physical therapists whose practice involves systems dependent on autonomic functions.

Wilfrid Jänig is Professor Emeritus of Physiology at the Christian-Albrechts University in Kiel, Germany. He has conducted neurobiological research on the autonomic nervous system since 1973. He combined research in Kiel with research at universities in Australia (Brisbane, Melbourne, Sydney), at the Hebrew University in Jerusalem, and at the University of California, San Francisco. His experiments, in which electrical signals in single sympathetic nerve fibers were recorded during natural and reflex activity, have established the principle of selective control of peripheral organs by the brain and the involvement of the sympathetic nervous system in various types of pain and in inflammation.

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> "This is the ultimate resource for anyone interested in autonomic neurosciences. Professor Jänig has tastefully updated a classic book which manages to distill a vast body of knowledge that will continue to be cherished by students as well as established scientists."

> Kalyanam Shivkumar MD PhD, Professor of Medicine, The University of California, Los Angeles (UCLA), and President, International Society for Autonomic Neuroscience (ISAN 2022)

> "Wilfrid Jänig has produced an outstanding synthesis of the state of knowledge of the autonomic nervous system (ANS). The book is far more than a summary of knowledge; Jänig has drawn out important principles from experimental work and his deep understanding of physiology. He shows how the ANS, in partnership with endocrine hormones, purposefully maintains cells, tissues, and organs in their optimal functional states.

> He points out that the definitions of the sympathetic and the parasympathetic nervous systems are based on the specialized anatomical arrangement of the autonomic outflow from the central nervous system to peripheral target tissues. Jänig points out forcefully that to speak of sympathetic or parasympathetic 'functions' generates misunderstandings and gives the wrong impression of how the ANS works. He writes instead of the many function-specific autonomic pathways (channels) that supply controls to tissues and organs. Jänig discusses in detail the old, but persistent, idea of a type of unitary discharge of the 'sympathetic' (or 'parasympathetic') system, which he concludes to be counter to what actually occurs. A nuanced ANS control dependent on sensory information from all organs, and the environment, as well as on emotional influences, is explained, that is, The Integrative Action of the Autonomic Nervous System to maintain bodily homeostasis.

The book is beautifully illustrated, especially with diagrams of autonomic circuits. Also very helpful are the conclusions paragraphs at the ends of chapters.

The book is essential reading for the seriously engaged physiologist and physician."

John B. Furness, Professor of Anatomy and Physiology, The University of Melbourne and The Florey Institute of Neuroscience and Mental Health

"For me, this is the 'Workshop Manual' of how the autonomic nervous system works. The *integrative* aspect of this book is quite superb. Jänig has avoided the traditional, and unhelpful, silo approach where bodily systems are separated in distinct chapters. This is inconsistent with how the body works. This new edition leaves no 'autonomic' stone unturned, covering endplates to emotion, credits the historical facts that have stood the test of time but kicks those into touch that have not. So pleasing was to see that the book challenges old/outdated dogma and sets the facts straight by reviewing the most current evidence. For instance, Jänig refutes respectfully Cannon's ideas on antagonism prevalence within the autonomic nervous system that corrupts so many of our students minds when reading their textbooks. I know that my copy of this book will spend its life being read and not on a shelf; it will be poured over by professors and students alike. The illustrations require a mention: they are exceptional - clear, concise, and comprehensive. I believe this book will put the autonomic nervous system front and center in the field of neuroscience."

Julian F.R. Paton PhD FRSNZ, Professor of Translational Physiology, University of Auckland, New Zealand

The Integrative Action of the Autonomic Nervous System Neurobiology of Homeostasis

Wilfrid Jänig Christian-Albrechts Universität zu Kiel, Germany



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> For UTE, my beloved wife. Without her this book would never have appeared in the World of Science

Contents

Foreword to the Second Edition ELSPETH M. MCLACHLAN	page xi
Foreword to the First Edition ELSPETH M. MCLACHLAN	xiii
Preface List of Abbreviations	xvii xix
Introduction: The Autonomic Nervous System and the Regulation of Body Functions Autonomic Adjustments of the Body and Behavior	n 1 1
Precision of Autonomic Regulation and its Failure in Disease Organization and Aims of the Book	2 4 5
PART I THE AUTONOMIC NERVOUS SYSTEM: FUNCTIONAL ANATOMY AND INTEROCEPTIVE AFFERENTS	7
Chapter I Functional Anatomy of the Peripheral Sympathetic	
and Parasympathetic Systems	9
1.1 Definitions and Limitations	9
1.2 Gross Anatomy of the Peripheral Sympathetic	
and Parasympathetic Nervous Systems	11
of Sympathetic and Parasympathetic Axons	18
1.4 Neuropeptides in Autonomic Neurons and the Idea	10
of "Neurochemical Coding"	22
1.5 The Peripheral Autonomic Nervous System in Submammalian	n
Vertebrates: A Comparative View	25
Little Brains and Sympathies	30
Chapter 2 Interoceptive Afferent Neurons and Autonomic	
Regulation with Special Emphasis on the Viscera	34
2.1 Visceral Primary Afferent Neurons: General Characteristics2.2 Visceral Primary Afferent Neurons as Interface Between Visce	35 eral
Urgans and Brain	39
 2.3 Receptive Functions of Visceral Afferent Neurons 2.4 Role of Visceral Afferent Neurons in Visceral Nociception and 2.5 Relation Between Functional Types of Visceral Afferent Neuron 	41 l Pain 48 ons,
Organ Regulation and Sensations	52

viii CONTENTS

2.6 (Central Ascending Pathways Associated with Autonomic Regulation and Body Interoception: A Generalization	56
PAR	T II FUNCTIONAL ORGANIZATION OF THE PERIPHERAL AUTONOMIC NERVOUS SYSTEM	71
Char	The Final Autonomic Pathway and its Analysis	71
Спар		/3
3.1	The Final Autonomic Pathway	73
3.2 1	of Integration	74
33	Activity in Perinheral Autonomic Neurons Reflects the Central	/4
0.0 1	Drganization	76
3.4 I	Reflexes in Autonomic Neurons as Functional Markers	77
3.5	Some Methodological Details About Recording From Peripheral	
1	Autonomic Neurons In Vivo	78
3.6 (Confounding Effects of Anesthesia in Animal Experiments	84
Chap	oter 4 The Peripheral Sympathetic and Parasympathetic Pathways	5 8 6
4.1 \$	Sympathetic Vasoconstrictor Pathways	87
4.2 \$	Sympathetic Non-Vasoconstrictor Pathways Innervating Somatic	
7	Fissues	100
4.3	Sympathetic Non-Vasoconstrictor Neurons Innervating	
]	Pelvic Viscera and Colon	109
4.4 (Other Types of Sympathetic Neuron	112
4.5 <i>I</i>	Adrenal Medulla	114
4.6	Sympathetic Neurons Innervating Immune Tissues	117
4.7 l	Proportions of Preganglionic Neurons in Major Sympathetic Nerves	120
4.8 l	Parasympathetic Systems	122
4.9 (Genetic-Molecular Aspects of Functional Differentiation	
(of Autonomic Neurons: A Summary	128
Chap	oter 5 The Enteric Nervous System	134
5.1 /	Anatomy, Components and Global Functions of the Enteric Nervous System	135
5.2	n its Own Right	1/1
5.3 l	Regulation of Motility and Intraluminal Transport in the Small	1-11
5.4 l	ind Large Intestines: The Neural Basis of Peristalsis Integration of Enteric Neural, Pacemaker and Myogenic	143
I	Mechanisms in Generation of Motility Patterns	148
5.5 l	Regulation of Secretion and Transmural Transport	154
5.6 l 5.7 (Defense of the Gastrointestinal Tract and Enteric Nervous System Control of the Enteric Nervous System by Sympathetic and	155
1	Parasympathetic Pathways	158

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PART III TRANSMISSION OF SIGNALS IN THE PERIPHERAL AUTONOMIC NERVOUS **SYSTEM** 165 **Chapter 6** Impulse Transmission Through Autonomic Ganglia 167 6.1 Morphology, Divergence and Convergence in Autonomic Ganglia 169 Strong and Weak Synaptic Inputs From Preganglionic Neurons 6.2 172 6.3 The Autonomic Neural Unit: Structural and Functional Aspects 179 6.4 Electrophysiological Classification, Ion Channels and Relation to Functions of Sympathetic Postganglionic Neurons 181 Different Types of Autonomic Ganglia and Their Functions In Vivo 6.5 184 6.6 Non-Nicotinic Transmission and Potentiation Resulting From Preganglionic Stimulation in Sympathetic Ganglia 192 **Chapter 7** Mechanisms of Neuroeffector Transmission 200 7.1 Transmitter Substances in Postganglionic Neurons 200 7.2 Principles of Neuroeffector Transmission in the Autonomic Nervous System 202 7.3 Specific Neuroeffector Transmissions 210 7.4 Integration of Neural and Non-Neural Signals Influencing Blood Vessels 217 7.5 Unconventional Functions of Sympathetic Noradrenergic Neurons 219 PART IV REPRESENTATION OF THE AUTONOMIC NERVOUS SYSTEM IN THE SPINAL CORD AND LOWER BRAIN STEM 227 Chapter 8 Anatomy of Central Autonomic Systems 231 8.1 Tools to Investigate the Anatomy of the Central Autonomic Systems 231 8.2 Morphology and Location of Preganglionic Neurons 234 8.3 Nucleus Tractus Solitarii 245 Sympathetic and Parasympathetic Premotor Neurons in the Brain Stem and Hypothalamus 249

Chapter 9Spinal Autonomic Systems2619.1The Spinal Autonomic Reflex Pathway as a Building Block
of Central Integration2619.2Spinal Reflexes Organized in Sympathetic Systems2649.3Sacral Parasympathetic Systems2729.4Autonomic Dysreflexia Chronically After Spinal Cord Transection2839.5The Spinal Cord as an Integrative Autonomic Organ285

X CONTENTS

Chapter I	Regulation of Organ Systems by the Lower Brain Stem	292
10.1 Genera 10.2 Sympat	l Functions of the Lower Brain Stem hetic Premotor Neurons in the Ventrolateral Medulla	293
Oblong	ata	294
10.3 Barored	eptor Reflexes and Blood Pressure Control	309
10.4 Arterial Neuron	Chemoreceptor Reflexes in Sympathetic Cardiovascular	318
10.5 Sympat	hetic Premotor Neurons in the Caudal Raphe Nuclei	321
and Reg	rulation of Respiration	374
10.7 Vagal E	fferent Pathways and Regulation of Gastrointestinal	524
Functio	ins	339
Chapter I	I Integration of Autonomic Regulation in the Upper Brain Stem and Limbic–Hypothalamic Centers:	255
	A Summary	355
11.1 Functio	ns of the Autonomic Nervous System: Cannon and Hess	355
11.2 Genera 11.3 Autono	n Aspects of Integrated Autonomic Responses mic Responses Activated Quickly During Distinct Behavioral	361
Pattern	S	365
11.4 Emotio	ns and Autonomic Reactions	378
11.5 Integra	tive Responses Organized in the Hypothalamus	384
11.6 Synops	is: The wisdom of the Body Revisited	391
Epilogue	The Autonomic Nervous System in Future Research:	
	Some Personal Views	397
	WILFRID JÄNIG, ELSPETH M. MCLACHLAN	
Index		403

All references cited in the text are available online at www.cambridge.org/janig.

Foreword to the Second Edition

Elspeth M. McLachlan, Prince of Wales Medical Research Institute and the University of New South Wales, Sydney, NSW, Australia.

Cardiac and smooth muscles, exocrine glands, fat stores, primary and secondary immune organs, etc. throughout the bodies of vertebrates are innervated by autonomic pathways. The first edition of Wilfrid Jänig's book The Integrative Action of the Autonomic Nervous System (2006) brought together what was known about the anatomy, physiology and pharmacology of this system, at the level of organs, tissues and cells. The book has become the mainstay of current information on the neural control of autonomic function. In the first edition, Wilfrid compiled and extended knowledge of how central nervous integration is transformed within sympathetic and parasympathetic pathways to regulate the peripheral organs and tissues, including the cellular mechanisms by which the central signals are transmitted to the effector tissues. Information about research in autonomic function, using classical and modern techneurophysiology, niques in neuroanatomy, pharmacology and biochemistry, was integrated with the fundamental understanding of this system accumulated over more than 100 years and summarized in a complete and accessible way.

Over many years, Wilfrid's own laboratory has concentrated on the ongoing and reflex electrophysiological activity of sympathetic outflows, mainly postganglionic, in limb and visceral nerves supplying a variety of organs. Recently they have examined the effects of nerve injury on this activity, and the mechanisms underlying neuropathic pain. In addition, Wilfrid has recruited an international autonomic community to analyze at a cellular level, using cellular anatomy and topography, neurochemistry, ganglionic and neuroeffector transmission, and sympathetic involvement in nociception and inflammation. The results of this research by him and his collaborators underpin the philosophy of his book. However, his wider interests encompass the central pathways involved in the control of autonomic outflows and he has sought to synthesize what is known about these pathways as well. Gaps in knowledge have been defined and the most significant questions to be answered clearly identified.

In the 16 years since the first edition, many of the important questions have been addressed using newer techniques in molecular biology, genetic manipulation and ontogenetics, and it is time to reevaluate the material. This new edition of the book incorporates many of the more recent data into the stories told in the previous edition and outlines the new ideas that have been developed over this period. The questions still to be answered have been reconsidered and are posed for the current cohort of researchers to investigate.

Wilfrid has spent half a century lecturing to medical students, postgraduate researchers and clinical practitioners about the functioning of the autonomic nervous system and the results of modern research. His expertise in concisely summarizing the concepts in each area of study with simple clear diagrams reflects this long experience and the popularity of his approach. He has not only trained dozens of medical and science graduates in the methodology of research, but has also written, revised and updated many chapters in textbooks addressed to the next generation of basic and clinical physiologists. This combination of teaching and research was much influenced by his interactions with Robert Schmidt, his mentor at the onset of his career in the 1960s, and follows the German tradition of the "unity of research and teaching" (Einheit von Forschung und Lehre) formulated and propagated by Wilhelm von Humboldt. This second edition has benefitted from this extensive experience in rethinking and improving the contents of this very valuable and comprehensive book. This revised and updated version will bring Wilfrid's special interpretation of current knowledge of the regulation of autonomic function to the next generation of readers.

Foreword to the First Edition

Elspeth M. McLachlan, Prince of Wales Medical Research Institute and the University of New South Wales, Sydney, NSW, Australia.

The autonomic nervous system carries the signals from the central nervous system to all organs and tissues of the body except skeletal muscle fibers. It is made up of preganglionic and postganglionic neurons linked together in functionally distinct pathways. The postganglionic terminals have specific relationships with their target tissue. As well as distributing centrally derived command signals, this system can also integrate reflex interactions between different parts of the peripheral nervous system, even without involving the spinal cord. All of these activities are specific for each organ system and attempts to generalize have often proved incorrect. The breadth and scope of involvement of this system in body function are obvious. The autonomic nervous system controls not only the quantity and quality of tissue perfusion in response to varying needs, and the maintenance of secretions for protection of the body's orifices and the lining of the gastrointestinal tract, but it also regulates the usually intermittent but complex functions of the abdominal viscera and pelvic organs, the mechanical aspects of the eye and the communication between the nervous system and the immune system. Many autonomic pathways are continuously active but they can also be recruited when the environmental and/or emotional situation demands it. This system is essential for homeostasis hence the subtitle of this book.

Despite its enormous importance for the maintenance of normal physiology in all vertebrate species, and for the understanding of many clinical symptoms of disease, the autonomic nervous system has not, even transiently, been the center of attention in neuroscience research internationally over the past 40 years. Many seem to think that this system has been worked out and there is nothing new to investigate. The discovery of neuropeptides as putative transmitters was probably the only interlude that triggered widespread excitement. Others simply forget that the system exists except for emergencies. Two views about the autonomic nervous system are often encountered:

- 1. that this system is similar to the endocrine system and its functions can all be explained by the pharmacological actions of the major neurotransmitters, noradrenaline and acetylcholine, possibly involving modulation by cotransmitters and neuropeptides, or
- **2.** that the functions of this system are not important as life continues without them.

For anyone who thinks about it, at least the latter of these concepts is obviously not true. Life can be maintained in a cocoon in individuals with autonomic failure but the ability to cope with external stressors severely compromises their quality of life. The extent to which the practical difficulties of daily life for people with spinal cord injury, which disrupts the links between the brain and the autonomic control of the body's organs, absorb personal energy and resources should not be underestimated by those who take their bodies for granted. Elderly people face similar problems as some of their autonomic pathways degenerate.

On the other hand, the former of the above two concepts dominates almost all current textbooks of physiology and neuroscience. It is true that some of the effects of autonomic nerve activity can be mimicked by the application of neurotransmitter substances locally or systemically. However, the mechanisms by which the same substances released from nerve terminals produce responses in the target tissue have proved to be quite different in most cases so far analyzed. This helps to explain the failure of many pharmaceutical interventions based on this simplistic idea as outlined above. What is important here is that the present volume collates the evidence against both these ideas and develops the factual and conceptual framework that describes how an organized system of functional nerve connections that operate with distinct behaviors is coordinated to

xiv FOREWORD TO FIRST EDITION

regulate the workings of the organ systems of each individual.

Nevertheless, over the past 40 years, there have been remarkable strides in our understanding. Technical problems limit how the complexities of this system can be unraveled. There are enormous challenges involved in investigating a complex interconnected system made up of small neurons that are not always packaged together in precisely the same way between individuals. Even in the spinal cord, the neuroanatomical distribution and apparent imprecision have been daunting. To study this system requires patience and persistence in the development of manipulative and analytical skills. These attributes are relatively rare.

Fortunately, over this period, a small but steady stream of researchers has persisted in their endeavors to clarify how this functionally diverse system works. One of the most significant players has been Wilfrid Jänig. Wilfrid and his many students and collaborators at the Christian-Albrechts-Universität in Kiel have pursued a major and uniquely productive approach to understanding how sympathetic pathways work. This has been to apply the technique of extracellular recording from single identified axons dissected from peripheral nerves projecting to particular target tissues and therefore acting in known functional pathways. Over the 40 years, this work, originally in cats and latterly in rats, has revealed the principles underlying reflex behavior of sympathetic axons in the anesthetized animal. The characteristic behavior of pre- and postganglionic neurons in over a dozen functional pathways has been defined. As the reader progresses through the book, it will become clear that many of these reflexes are also present in humans. The parallel technique of microneurography, pioneered by Hagbarth, has been implemented over a similar period in the sympathetic pathways of conscious humans by Gunnar Wallin and his colleagues in Göteborg. While pathways to the viscera are currently too hard to study in humans because they are less accessible, the principles of their organization can be deduced from Wilfrid's data on pre- and postganglionic discharge patterns and from the analyses of ganglionic and neuroeffector transmission conducted by him and others.

Over the 40 years, Wilfrid's various interests have been broad but always focused. They have taken him to many places to answer questions about the structure and function of sympathetic pathways. His earliest training in single unit recording was in sensory neurophysiology and this background has been the basis of his parallel studies of visceral afferent behavior and nociception. Early in his career, he was interested in integrative autonomic control at the higher levels of the nervous system and developed a passion to follow on the work of Philip Bard. After returning to Germany from New York in the 1970s, he conducted experiments on decorticate and decerebrate cats in which he created behaviors such as sham rage during which he planned to record and analyze the sympathetic outflow. These experiments did not progress because of limited resources, but instead he undertook a most detailed analysis of the distinctive behavior of skin and muscle sympathetic vasoconstrictor axons. These results provided evidence that strongly rejected popular ideas that a general level of "sympathetic tone" was the determinant of peripheral vascular resistance. It was clear that the reflex connectivity of the pathways involved in cutaneous and skeletal muscle blood flow are largely independent. This concept was more dramatically confirmed in recordings from humans where it is possible to demonstrate the strong emotional drive that modulates cutaneous vasoconstrictor activity (see Subchapter 4.1.2 in this book). Subsequently Wilfrid's laboratory has extended this type of analysis to over a dozen different pathways that they have studied in anesthetized animals.

I first met Wilfrid in 1979 when he came to give a seminar in Edinburgh where I was on sabbatical leave at the time. As my original background was in cardiovascular physiology, I had naturally read his work on vasoconstrictor discharge patterns and had lots of questions to ask him. Wilfrid invited me to visit Kiel on my way home (it was very cold and wet in November) and then he came to Melbourne to work with me to trace the peripheral sympathetic pathways quantitatively. In my laboratory at Monash University, I had established the retrograde tracing technique using horseradish peroxidase to identify the location of preganglionic neurons in the spinal cord as a prelude to recording intracellularly from them. He worked hard with me cutting and mounting thousands of sections and soon after I spent a similar period in Kiel helping his group establish the technique there. This quantitative work dovetailed well to explain how the axons that his group sampled in their recordings related to the entire population.

FOREWORD TO FIRST EDITION xv

It has been my great privilege to continue to work with Wilfrid and his colleagues, particularly up to the early 1990s, undertaking studies for which he and I received the Max-Planck Forschungspreis for international collaboration in 1993. Since that time, and in various parts of Australia as I have moved between universities, we have worked together and in parallel on aspects of the interactions between the sympathetic and sensory systems that may be involved in neuropathic pain after nerve injury. We have continued to communicate frequently and his younger colleagues, notably Ralf Baron, Ursula Wesselmann and Joachim Häbler, have spent time in Australia working in my laboratory. I hope and expect that these interactions will continue.

Wilfrid's early studies of sympathetic activity were made when Robert Schmidt was in Kiel and were conducted in parallel with studies of somatosensory, particularly nociceptive, afferents. This anteceded his interest in visceral afferent function to which he applied the same technical expertise to unravel the behavior of these neurons, particularly in pelvic organ reflexes. His interests in nerve injury were pursued in part with Marshall Devor in Jerusalem. This involved extended studies of the ectopic activity of sensory neurons after peripheral nerve lesions and the role of sympathetic activity in triggering this. His laboratory has also conducted a wide range of studies on the effects of various nerve lesions on the properties of sympathetic and afferent axons. As Wilfrid appreciated that the problem of neuropathic pain was probably related to inflammation, he sought out Jon Levine in San Francisco where he was exposed to a very strong research community involved in pain and inflammation research. He has a prodigious output from Jon's laboratory deciphering the components of the neuroimmune interactions using rigorous and systematic approaches to identify the pathways and sites at which the hypothalamo-pituitary-adrenal axis (HPA) intervenes in inflammation and in nociception, in some cases with sympathetic involvement. More recently, Wilfrid and Ralf Baron have worked with the clinical community worldwide on clarifying the misnamed concept of "reflex sympathetic dystrophy" and developing the newer definitions of various "complex regional pain syndromes" to help to clarify the diagnosis of the mechanisms underlying chronic neuropathic pain.

When visiting my laboratories at Monash and the Baker Institute in Melbourne, and subsequently at the Universities of New South Wales and Queensland, and more recently at the Prince of Wales Medical Research Institute in Sydney, Wilfrid has been able to visit many neuroscientists around Australia where research on the neurobiology of the autonomic nervous system and on central cardiovascular control is prolific by world standards. He has seized upon these opportunities to learn what the community of Australian autonomic researchers is doing and has established strong relationships with the leaders of many active laboratories including those of David Hirst, Ian Gibbins and Judy Morris, John Furness, Marcello Costa, Christopher Bell, Janet Keast, Sue Luff, James Brock, Roger Dampney, Robin McAllen, Bill Blessing, Paul Korner, Dick Bandler, Paul Pilowsky and Dirk van Helden. This extensive Australian involvement in autonomic neuroscience arose in part from the students who trained with Geoff Burnstock and Mollie Holman in Melbourne in the 1960s and 1970s and who have taken their skills across the country and have been training the next generations since that time. Despite the divergence of their specific interests, this community continues to be one of the largest internationally working in the autonomic nervous system. Wilfrid's exposure to the cellular, pharmacological and neuroanatomical aspects of ganglionic and junctional transmission in the peripheral pathways gave him a very wide view of autonomic effector systems, which he has so cleverly incorporated into this book.

Throughout these years, Wilfrid has been a prodigious author of textbook chapters and review articles. Although many of the former have been written in German, he has also developed and expounded his ideas about neural control of vasoconstriction, pain and the sympathetic nervous system, the consequences of nerve injury, the involvement of the HPA axis in inflammation and nociception, and on clinical aspects of these topics. This book arises from this lifetime of synthetic writing and from his reflection on the wider issues of this area of science. It also is the product of his frustration, which I share, with the limited availability of publications that summarize the scientific background and present the current status of our understanding of how the autonomic nervous system works. As in his experiments, he has dissected the system into the major functional pathways in which reflex behavior and cellular

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xvi FOREWORD TO FIRST EDITION

mechanisms have been well investigated. He reviews and synthesizes the available information on the spinal cord and brain stem components of autonomic reflexes and then re-synthesizes these output systems into a complex package that includes the control of autonomic discharge patterns from the midbrain and higher centers. He has extracted the key information yielded by both classical and modern technical approaches used to study these components of the nervous system. He has incorporated the conceptual background behind each area of research. Finally, he discusses how the old "unifying" concepts of Cannon and Hess misrepresented the diversity of autonomic outflow patterns that the brain recruits during the various behaviors that function to conserve the body in a range of environmental circumstances. This philosophical base needs to replace the widely held views mentioned earlier if we are to progress our understanding of this important set of control systems. The present tour de force has involved discussion and input from many of Wilfrid's collaborators and colleagues around the world whose contributions have ensured that the final product really contains the most up-to-date summary of our current knowledge of autonomic function.

Despite, or because of, this diversity of inputs, this book provides Wilfrid Jänig's unique overview of the autonomic nervous system. Without his driving fascination with how the whole autonomic system works in the body, this book would never have been written. No-one else currently has the conceptual breadth and capacity to integrate so many aspects to compose this amalgam. He has collected all the available data from the past and the present and fitted them together with what is known of the central control and spinal integration that determine the activity patterns in each outflow pathway. He has taken the knowledge from Langley's time, through Cannon, Hess and Bard, Burnstock and Holman, to the recent application of cellular biology and molecular genetics to collate a truly comprehensive compendium. I am delighted that he has committed himself to drawing together so many diverse aspects of autonomic function in one place and to give us a truly integrated overview of what is known at the beginning of the twenty-first century. He has made very clear what he feels are the major questions that remain to be answered. I know that Wilfrid will contribute to many of those answers.

Preface

In the late 1960s, while I was working in Robert F. Schmidt's laboratory in the Department of Physiology of the University of Heidelberg, conducting experiments on cutaneous primary afferent neurons and presynaptic inhibition in the spinal cord, Robert introduced me to the sympathetic nervous system. We worked on somatosympathetic reflexes and other spinal reflexes, some of the work being conducted with Akio Sato. At this time, I tried to understand The Wisdom of the Body by Walter Bradford Cannon (Cannon 1939) and Vegetatives Nervensystem by Walter Rudolf Hess (Hess 1948). However, from 1971 to 1974, I continued with my experimental work on the somatosensory system and concentrated with Alden Spencer on the cuneate nucleus and thalamus in the Department of Neurobiology and Behavior of the Public Health Institute of the City of New York (directed by Eric Kandel).

While working in New York I came into contact with Chandler McCuskey Brooks (Downstate Medical Center, State University of New York). He invited me to attend the Centennial Symposium "The Life and Influence of Walter Bradford Cannon, 1871-1945: The Development of Physiology in this Century" (Brooks et al. 1975). Chandler encouraged me to concentrate scientifically on the autonomic nervous system; he remained very supportive until his death 17 years later. This influence and particularly the books of Cannon and Hess led to my decision to leave the somatosensory field and redirect my research, after my return to Germany, to investigations of the sympathetic nervous system. The books by Cannon and Hess, and the published papers on which they are based, aroused from the beginning my opposition on the one hand and my secret admiration for these authors on the other. This ambiguity in my scientific attitude towards Cannon and Hess has always been in the background of the scientific activities in my laboratory, of my teaching and of my writing on the autonomic nervous system.

I am particularly grateful to two persons who have kept me going on the scientific path amidst trials and tribulations to unravel some of the mysteries of the autonomic nervous system. Robert Schmidt has made me invest time in writing textbook chapters on the autonomic nervous system since 1971. Elspeth McLachlan has always been extremely supportive and virtually carried me through some periods of doubt and despondency throughout the 40 years we have worked experimentally and scientifically together. She introduced me to Australian Autonomic Neuroscience and is responsible for this book being in some ways an Australian book (see below). Finally, the many young students in my laboratory, some now professors, influenced me by their enthusiasm despite my being entirely uncompromising, which was sometimes hard for them to digest.

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I want this book to be a forum for ongoing discussion. I strongly encourage young scientists to invest their time in research on the autonomic nervous system. While writing the book I was in continuous discourse with many scientists in Australia, Europe and the United States addressing various scientific aspects of the book. These scientists have made a major contribution.

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xviii | PREFACE

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Abbreviations

The main abbreviations used are listed below. Special abbreviations related to anatomical structures in the lower brain stem or hypothalamus are listed in the legends of the figures and tables, particularly Figures 10.2, 11.13, 11.14 and Tables 8.2 and 8.3.

gends of the figures a gures 10.2, 11.13, 11.14 ar	ls of the figures and tables, particularly es 10.2, 11.13, 11.14 and Tables 8.2 and 8.3.		cyclic guanosine monophosphate	
AC	anterior commissure	CGRP	calcitonin gene-related peptide	
ACC	anterior cingulate cortex	ChAT	choline acetyltransferase	
ACh	acetylcholine	Cl	internal carotid artery	
Ag/AgCl	silver-silver chloride	CL/cl	centrolateral nucleus	
AG	antigen		(thalamus)	
AHN	anterior hypothalamic nucleus	CM	circular musculature (gastrointestinal tract)	
AM	adrenal medulla	CNIS	central nervous system	
	arcuate nucleus		common carotid arteny	
	autonomic nervous system	CPA		
	autonomic neural unit	CFA CPC		
	area postrema	CKG	central respiratory	
AIP	adenosine triphosphate	СРЦ	generatoria releasing	
BAI	brown adipose tissue	CRH	bormone	
BC	bulbocavernous (muscle)	CDDC		
BL/INF	factor	CNFS	syndrome	
RV	bradykinin	CSN	carotid sinus nerve	
		CSP	carotid sinus pressure	
BIIIP	bone morphogenetic	CST	cervical sympathetic trunk	
BN	Barrington's nucleus	CT	chromaffin tissue	
BNST	bed nucleus of the stria	CTh	cholera toxin subunit B	
	terminalis	CVC		
BötC	Bötzinger complex	CVC	vasoconstrictor	
BP	blood pressure		(neuron)	
BV	blood vessel	CVD	cutaneous vasodilator	
c, C	cervical (segment)	0.0	(neuron)	
CA	central autonomic nucleus	CVLM	caudal ventrolateral medulla	
Ca ²⁺	calcium ion	cVRG	caudal ventral respiratory	
cAMP	cyclic adenosine		group	
CBE	cerebral blood flow	CVS	cardiovascular system	
	central canal	DA	dopamine	
CC	corpus callosum	DBH	dopamine- β -hydroxylase	
ССК	cholecystokinin	DC	dorsal column (spinal cord)	
CE	external carotid artery	DCN	dorsal commissural nucleus (spinal cord)	

CeAM

CG

central nucleus of the

amygdala

celiac ganglion

XX LIST OF ABBREVIATIONS

DH	dorsal horn (spinal cord, trigeminal)	GiV	gigantocellular reticular
DLF	dorsolateral funiculus	GLP-1	glucagon-like peptide l
DMH or DM	(spinal cord) dorsomedial hypothalamus	GnRH	gonadotropin-releasing
DMN	dorsomedial nucleus (of the hypothalamus)	GR	gray ramus
DMNX	dorsal motor nucleus of	GSR	galvanic skin response
	dihydroxyphenylalanine	HGN HPA axis	hypogastric nerve hypothalamo–pituitary–
DR	dorsal posterior insula dorsal root	НРС	adrenal axis
DRG	dorsal root ganglion		heart rate
DVC	dorsal vagal complex		herendish perovidase
DYN	dynorphin	5_HT	5-bydroxytryptamine
ECG	electrocardiogram	5111	(serotonin)
EJC	excitatory junction current	HVPG	hypothalamic visceral pattem generator
EJP	excitatory junction	IAS	intrinsic anal sphincter
	potential	IC	intercalated spinal nucleus
el	external lateral nucleus	ICC	interstitial cell of Cajal
EMG	(parabrachial complex) electromyogram	ICNS	intrinsic cardiac nervous
ENDC	endocrine cell	IFG	immediate early gene
ENK	enkephalin	IGL	intraganglionic laminar
ENS	enteric nervous system	102	ending (enteric nervous system)
EPSC	excitatory postsynaptic current	IJР	inhibitory junction potential
EPSP	excitatory postsynaptic	IL	interleukin
FLIC	potential	ILf	funicular part of the
EUS	external urethral sphincter		intermediolateral
	nucieus Edinger-VVestphal		nucleus
fd FG	Fast Blue Fluoro-Gold	ILp	principal part of the
FN	facial nucleus		Intermediolateral
GABA	γ-aminobutyric acid	IMA	intramuscular array (enterio
GAL	, , , , , , , , , , , , , , , , , , ,		nervous system)
GALT	gut-associated lymphoid tissue	IMG	inferior mesenteric ganglion
GH	growth hormone	IML	intermediolateral nucleus
GHRH	growth hormone- releasing hormone	IN	(spinal cord) interneuron
GiA	gigantocellular reticular nucleus aloba	INA INCS	integrated nerve activity
GIT	gastrointestinal tract		intrinsic cardiac nervous system

LIST OF ABBREVIATIONS xxi

INS	inspiratory/inspiration-	LT	low threshold
	type sympathetic	LTB	leukotriene B
	neuron	LTC	leukotriene C
INSP	inspiratory/inspiration	LTF	lateral tegmental field
IO	inferior olive nucleus	MAP	mean arterial blood
IPAN	intrinsic primary afferent		pressure
	neuron (enteric nervous system)	MaSN	major splanchnic nerve
IP ₃	inositol	MBO	mammillary body
	1,4,5-triphosphate	MC	mast cell
IPS	inferior periinsular sulcus	MCC	middle cingulate cortex
IPSP	inhibitory postsynaptic	MCG	
	potential	MDura	ventral partian of the
IRH	inhibitory releasing hormone	ΠDVC	medial dorsal nucleus (thalamus)
i.v.	intravenous	ME	(trialarios)
IVLM	intermediate		
	ventrolateral medulla	MIEPO	median preoptic nucleus
IZ	intermediate zone (spinal	MISIN	minor splanchnic nerve
	cord)	MMC	migrating myoelectric
JGA	juxtaglomerular apparatus (kidney)		complex (enteric nervous system)
KF	Kölliker–Fuse (nucleus)	MP	myenteric plexus (enterio
I, L	lumbar (segment)		nervous system)
LAH	long afterhyperpolarization	MPN	medial preoptic nucleus
LC	locus ceruleus	MR	motility-regulating
LCN	local circuit neuron		(neuron)
LF	lateral funiculus (spinal cord)	mRNA	messenger ribonucleic acid
LFN	lateral funicular nucleus	MVC	muscle vasoconstrictor
LH	lateral hypothalamus		(neuron)
LHA	lateral hypothalamic area	MVD	muscle vasodilator
LHRH	luteinizing-hormone-		(neuron)
	releasing hormone	Ν	neurotensin
LM	longitudinal musculature	NA	nucleus ambiguus
	(enteric nervous system)	NA _C	compact formation of the NA
LPGI	nucleus paragigantocellu- laris lateralis	NA _e	external formation of the NA
LPN	lateral preoptic nucleus	NA.	loose formation of the
LPS	lipopolysaccharide	· · · · L	NA
LRN	lateral reticular nucleus	NAcc	subcompact formation of
LSN	lumbar splanchnic nerve	· · · · SC	the NA
LST/LSC	lumbar sympathetic trunk/lumbar	nAChR	nicotinic acetylcholine receptor
	sympathetic chain	NAd	noradrenaline
	/ 1		nor adi Challine

xxii LIST OF ABBREVIATIONS

NANC	non-adrenergic non- cholinergic	PMC	pontine micturition center
NAR	nucleus arcuatus	PMNL	polymorphonuclear
NFP	neurofilament protein		leukocyte
NKI/NKA	neurokinin I/A	PINMI	phenylethanolamine-
NMDA	N-methyl-D-aspartate		N-methyl transferase
	(acid)	PP	pancreatic polypeptide
NO	nitric oxide	preBötC	preBötzinger complex
NOS	nitric oxide synthase	PRV	pseudorabies virus
NPY	neuropeptide Y	PSC	pontine storage center
NS	nociceptive specific (neuron)	PSCN	presuprachiasmatic preoptic nucleus
NSF	N-ethylmaleimide-	PSDC	postsynaptic dorsal column
	non a terminal action	PSN	pelvic splanchnic nerve
INTAL	nerve terminal action	PT	primary transmitter
NTS	nucleus tractus solitarii	PVH	paraventricular nucleus o the hypothalamus
NTS _{cen}	pars centralis of the NTS	PYY	pentide YY
OT	optic tract	REM	rapid eve movement
OVLT	organum vasculosum	RESP	respiration
	laminae terminalis	RH	releasing hormone
PACAP	pituitary adenylate	RN	raphe nuclei
	cyclase-activating	RNA	ribonucleic acid
	peptide	Rob/pal	raphe obscurus/pallidus
PaCO ₂	arterial CO_2 pressure	RVC	renal vasoconstrictor
PAF	platelet-activating		(neuron)
	factor	RVLM	rostral ventrolateral
PAG	periaqueductal gray		medulla
PAN	primary afferent neuron	rVRG	rostral ventral respirator
PaO ₂	arterial O_2 pressure		group
para	parasympathetic	s,S	sacral (segment)
PBC/PB	parabrachial complex/	SAH	synaptic
PCM	parabrachial nucleus	CALT	aπernyperpolarization
	parasympathetic cardio- motor (neuron)	SALT	skin-associated lymphoid tissue
PE	plasma extravasation	SCG	superior cervical ganglion
Pf	parafascicular nucleus (thalamus)	SCM	sympathetic cardiomotor (neuron)
PGE	prostaglandin E	SCN	suprachiasmatic nucleus
	posterior hypothalamic	SCO	subcommissural organ
PHA			0
PHA	area	sEPSP	slow excitatory
PHA PHA-L	area phaseolus vulgaris leuko- agglutinin	sepsp	slow excitatory postsynaptic potential
PHA-L PHR-L	area phaseolus vulgaris leuko- agglutinin phrepic pep/e	sEPSP SEPT	slow excitatory postsynaptic potential septum

LIST OF ABBREVIATIONS xxiii

S.E.M	standard error of mean	VH	ventral horn (spinal cord
SFO	subfornical organ	VIP	vasoactive intestinal
SG	stellate ganglion		peptide
SI	primary somatosensory cortex	\vee	ventrolateral nucleus (parabrachial)
SII	secondary	VLM	ventrolateral medulla
sIPSP	somatosensory cortex	VM/VMN	ventromedial nucleus (hypothalamus)
	postsynaptic potential	VMH	ventromedial
SIS	skin immune system		hypothalamus
SK channel	small-conductance	VMM	ventromedial medulla
	Ca ²⁺ -activated channel	VMb	basal part of the
SKP	skin potential		ventromedial nucleus
SKT	skin temperature		(thalamus)
SM	sudomotor (neuron)	VMpo	posterior part of the
SMC	smooth muscle cell		(thalamus, primate)
SMP	submucosal plexus (enteric nervous system)	VPI	ventral posterior inferior
som	somatostatin	\/DI	ventral posterior lateral
SP	substance P	VIL	nucleus (thalamus)
SPL	splanchnic nerve	VPM	ventral posterior
Sp5	spinal trigeminal nucleus	VI I I	medial nucleus
sp5	spinal trigeminal tract		(thalamus)
SS	somatostatin	VPpc	ventral posterior
STT	spinothalamic tract		parvicellular nucleus o
Sy	sympathetic		the thalamus (rat)
t,⊤	thoracic (segment)	VR	ventral root
TH	tyrosine hydroxylase	VRC	ventral respiratory
ТК	tachykinin		column
TNF	tumor necrosis	VRG	ventral respiratory group
	factor	VTA	ventral tegmental area
TRH	thyrotropin-releasing	VVC	visceral vasoconstrictor
	hormone		(neuron)
TRP	transient receptor potential		wide dynamic range (neuron)
TS	tractus solitarius	WHBP	working-heart-brain-ster
TTX	tetrodotoxin		preparation
UB	urinary bladder	WR	white ramus
VAChT	vesicular acetylcholine	X	vagus nerve/nucleus
	transporter	ZI	zona incerta