Contents

Acknowledgments .................................................................. VII
Preface ............................................................................... IX

Classical Neurotransmitters Role in Pain Control

Pert, A. (Bethesda, Md.): Cholinergic and Catecholaminergic Modulation of Nociceptive Reactions. Interactions with Opiates ......................... 1
Besson, J.M.; Chaouch, A. (Paris): Descending Serotonergic Systems ............ 64
Kuraishi, Y.; Satoh, M.; Takagi, H. (Kyoto): The Descending Noradrenergic System and Analgesia ................................................. 101

Opioid Systems and Analgesia


Contents VI

Non-Opioid Peptides and Analgesia:
Focus on Cholecystokinin

Noel, M.; Nemeroff, C.B. (Durham, N.C.): The Role of Nonopioid Peptides in Pain 194
Suberg, S.N.; Watkins, L.R. (Davis, Calif.): Interaction of Cholecystokinin and Opioids in Pain Modulation ................................. 247

Activation of Endogenous Mechanisms of Analgesia
Preface

The identification of the neurotransmitters of pain is perhaps one of the most significant obstacles impeding the development of effective analgesia-inducing drugs or therapeutic modalities. Although many advances in our understanding of this topic have been made in recent years, we still are in search of a magic bullet against pain. Our purpose in this volume has been to bring together the knowledge of various experts in the field of neurochemistry of pain and analgesia. Using biochemical, anatomical, and pharmacological tools, these researchers have attempted to understand the response to noxious stimuli (what we term pain) or the inhibition of the pain response (what we term analgesia). As the reader might expect, no one transmitter or modulator is uniquely responsible for either pain perception or pain inhibition. Indeed, almost every known brain transmitter when studied in relation to pain has been found to have some role. In some cases, such as opioid peptides, the case for an important role in pain modulation is reasonably strong and has face validity. For other substances, such as some of the newly discovered peptides, the case is less convincing, mostly because the investigation is in its early stages.

It is of course impossible to cover in one volume all the accumulated...
knowledge on the neurochemistry of pain modulation. Rather, we have attempted to give the reader an overview of the potential modulatory role of three main classes of neurochemical substances: (1) Classical neurotransmitters, such as catecholamines, serotonin and acetylcholine. (2) The opioid peptide family with the multiple products deriving from the opioid genes. (3) The nonopioid peptides, with a focus on one peptide in particular, cholecystokinin. In each of these three areas, we have included at least one chapter with a general overview of the field, as well as some chapters which detail a more discrete body of work focused on a particular subset of current questions. In this fashion we hope to provide the reader with two levels of information, a general appreciation of the current knowledge about each of these three classes of substances, and more specific examples of the type of research currently being performed in the area. Some of these examples reach paradoxical conclusions, may even be controversial, but they do challenge any illusion of a neat and tidy understanding of the biochemistry of pain control.

The last section of the book, rather than using specific neurochemicals as its starting point, focuses on known analgetic phenomena: acupuncture analgesia, stress-induced analgesia and stimulation-produced analgesia. The authors of these chapters, by summarizing work on the biology of analgetic phenomena, clearly point to the complexity of pain modulation, involving multiple anatomical sites of regulation, as well as multiple neurochemical systems. In so doing, they show us, from a different angle, both the complexity and dynamism involved in the mammalian response to painful stimuli.

There is a great deal this book does not deal with. Most notable is the question of the anatomical substrates integrating pain modulation, a topic ably covered in this series by the monograph of Dr. Willis. In addition, implications of the current biochemical information for human work and for the development of novel pharmaceutical agents is also left for future volumes in this series.

We are most grateful to the authors who have contributed to this collection. It is our hope that by presenting as one unit this overview of the biochemistry of pain modulation, we can allow a sharper perception of both the limitations and the power of this level of discourse. This, in turn, may ultimately cumulate in a better integration of all basic research on pain, and result in novel ways of controlling it.

H. Akil