Neurobiology of Obesity

Obesity is one of the prime contributors to ill health in modern society, affecting around 20–25% of the population. It can cause or exacerbate a variety of health problems and is often associated with several other diseases including type 2 diabetes, coronary heart disease and certain types of cancer. Significant progress has been made in understanding the role of the nervous system and, in particular, the complex interplay between a range of orexigenic and anorectic agents within specific hypothalamic nuclei in the regulation of energy balance, appetite and adiposity. Several different neuronal pathways, neurotransmitters and hormones have been identified as major players in the regulation of feeding behavior and body weight and these are now being targeted as having therapeutic potential. Written for academic researchers and graduate students, Neurobiology of Obesity is a concise overview of recent developments in this field, written by leading international experts.

Jennifer Harvey is currently a Wellcome Research Career Development Fellow in the Department of Pharmacology and Neuroscience at the University of Dundee. The main focus of her research is to investigate the role of the endocrine peptides, leptin and insulin, in both normal and pathological function in extrahypothalamic regions of the brain, including the hippocampus and cerebellum.

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Neurobiology of Obesity

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Preface

In the twenty-first century, obesity affects around 20–25% of the population and it is now one of the prime contributors to ill health in modern society. Obesity can cause or exacerbate a variety of health problems and it is often associated with a number of other diseases including type II diabetes mellitus, coronary heart disease and certain types of cancer. The incidence of obesity and related diseases is steadily increasing such that obesity is now regarded as a global epidemic. In recent years, major advances have been made in determining the role of the central nervous system, in particular specific hypothalamic nuclei, in regulating energy balance. From such studies it is apparent that a highly intricate neural system involving a complex interplay between a range of orexigenic and anorectic agents controls food intake and body weight. Thus, a greater understanding of the key neurotransmitter molecules, their related signal transduction pathways and molecular targets, as well as the neuronal pathways that control release of these neurotransmitters is vital if novel therapeutic targets for the treatment of obesity and related diseases are to be uncovered. This book provides a concise overview of recent developments in this field. As an introduction, Professor Bloom gives an outline of the factors that are known to play a key role in regulating energy balance and the development of obesity in humans. Professor Clement considers the genetics of human and rodent body weight regulation as the use of genetic technologies has markedly increased our understanding of dysfunctions in body weight regulation. The hypothalamus is a key region of the brain that adjusts both the drive to eat and energy expenditure in response to a range of signals. Professor Ahima reviews the role of particular medial hypothalamic structures in this regulatory process, and introduces the concept that a range of distinct, but molecular signals interact to control food intake. In the following chapter, Dr Niswender reviews the evidence implicating leptin and insulin as key hormones that provide afferent information to the brain as well
as the recent advances made in determining the sites and mechanisms of action of these adipostats. This aspect is expanded on by Dr Sutherland and Professor Ashford, who provide an overview of the signaling capability of leptin and insulin receptors and discuss how specific signaling pathways may impact on feeding behavior. The potential development of specific therapeutic agents directed against signaling pathways regulated by leptin and insulin for the treatment of obesity is also discussed. This is followed by a detailed review by Dr Strack and Professor Levin of various animal models of diet-induced obesity and how these compare with human obesity. In addition to leptin and insulin, findings from both genetic and pharmacological studies have implicated melanocortins, opiates and the gut hormone ghrelin in hypothalamic regulation of energy homeostasis. The role of these agents is dealt with in depth in reviews by Professors Low, Levine and Horvath, respectively. Drs Della-Fera and Baile discuss the role of the CNS in regulating the levels of adipose tissue, whereas in the final review, Dr Halford provides a detailed overview of the therapeutic strategies to treat obesity.
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