

Preface

During the past decade studies have shown that growth hormone (GH) may exert profound effects on the central nervous system (CNS). The hormone thus appears to display an important role in many functions related to the CNS. GH deficiency is known to result in a reduction of several dimensions related to quality of life. However, exogenous compensation of the hormone may counteract these disabilities. For instance, GH replacement therapy is found to improve the psychological capabilities in adult GH-deficient (GHD) patients. Beneficial effects of the hormone on certain functions, including memory, mental alertness, motivation, and working capacity, have been reported. GH treatment of GHD children has also been observed to produce significant improvement in many behavioral problems seen in these individuals. Studies also indicated that GH replacement therapy affects the cerebrospinal fluid (CSF) levels of various hormones and neurotransmitters. Further support for CNS being a target for GH emerges from observations indicating that the hormone may cross the blood-brain barrier (BBB) and from studies confirming the presence of GH receptors (GHR) in the brain. Many effects of GH are mediated through the release of insulin-like growth factor-I (IGF-I). Therefore, studies on effects induced by IGF-I on brain function have been applied in order to obtain increased understanding of the mechanism by which GH exerts effects on brain areas related to various behaviors seen to be affected during GH replacement. The aim of this book is to summarize and highlight some recent knowledge in this area. This includes clinical observations of patients with a reduced ability to produce the hormone along with successful outcomes of GH replacement therapy in GHD patients and neuroprotective effects involving the somatotrophic axis, as well as animal models to explore the mechanisms at the neurochemical level by which the hormone induces its effects.

The first two chapters deal with some fundamental concepts regarding the biosynthesis and chemical nature of GH and IGF-I, focusing on mechanisms behind the regulation of secretion of these hormones to give the reader a brief background of events taking place in the body before the hormones interact with their receptors. The following two chapters describe basic mechanisms of how GH and IGF-I interact with receptors on their target cells. This includes text on receptor structure and mechanisms involved in signal transduction to finally give the GH or IGF-I response. Subsequent to these introductory chapters, the book content addresses questions related to the CNS.

Chapters 5 and 6 discuss mechanisms by which GH and IGF-I may reach their targets in the CNS. Also, methods for quantification and analysis of the two hormones in the CSF and their application in clinical studies are highlighted. Models used to study the transport of GH over the BBB are described. It seems that although there is strong evidence that GH may cross the BBB, as judged from human studies, it is difficult to demonstrate an active transport mechanism for the hormone using animal models. In human subjects, administration of GH causes a dose-dependent increase of the hormone in the CSF, whereas in models using rats or cell lines, penetration of the hormone across the BBB seems limited. As for IGF-I, it is demonstrated that this growth factor in conformity with insulin and prolactin may be transported over the BBB through a receptor-mediated mechanism.

An important part of the book content is given in Chapters 7–9, dealing with GH and IGF-I receptors in the brain regarding their regional distribution along with their chemical nature. Data on purification of GH receptors from human brain tissues, as well as description of the characteristic of GHR gene transcripts, are included in these chapters.

The outline of a procedure combining affinity chromatography and zone electrophoresis for the recovery of a purified preparation of GHR from the human choroid plexus is described in Chapter 8, and Chapter 9 deals with the characteristics of the GHR message in various regions of the rat brain. A comprehensive review on the localization of GH and IGF-I receptors is given in Chapter 7.

In the next section of the book there are a series of chapters (10–15) dealing with functional aspects of the role of the somatotrophic axis in the brain. Various types of animal models and cell systems have been used to establish a comparatively deep knowledge in functions that GH and IGF-I have in CNS injury, neurogenesis, and cognitive behaviors. Also, the interaction in various brain circuits of GH with prolactin is highlighted.

A major part of this book (Chapters 16–23) is directed to clinical studies. Hence, the role of the somatotrophic axis in acromegaly, life quality, psychiatric diseases, aging, and neurodegenerative diseases, e.g., Alzheimer's disease, is discussed. Also, the beneficial effects of hormone replacement GHD in children and GH-induced improvement on cognitive functions in elderly GHD patients are highlighted.

Finally, the remaining chapters focus on future perspectives, e.g., on the potential use of GH antagonists as possible pharmacological tools in future therapy and on future perspectives with respect to GH replacement therapy and life quality. Taken together, it has been interesting to see that it has been possible to get contributors to this book with such a good representation of geographical districts around the world, but also a good representation of the research around the world on the somatotrophic axis in relation to CNS.

It is believed that with the current advances in research on GH and IGF-I, this volume will represent a timely book that contributes an important topic that will be of interest to a variety of scientists from students and medical practitioners to basic and clinical researchers.

I am grateful to all my colleagues who have contributed such excellent chapters to this volume. As editor, I would like to point out that all these chapters were submitted within a time period of 6–7 months and should therefore contribute the very recent knowledge in the respective field covered within the volume.

Fred Nyberg
Uppsala in June, 2005