1. INTRODUCTION: THE CEREBELLUM AND ITS DISORDERS IN THE DAWN OF THE MOLECULAR AGE

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1. HISTORICAL BACKGROUND
The study of the cerebellum has a long and fascinating history, spanning many centuries. As Dow describes in his detailed historical review of cerebellar investigation [1], the Greek physician Herophilus (335–200 BC), known as the “father of anatomy,” is generally credited for recognizing the human cerebellum as a distinct brain division. About two millennia later, Sir Thomas Willis (1621–1675) made comparative anatomical observations drawing attention to the characteristic morphologic appearance of the cerebellum in vertebrates. It seems that these observations stimulated interest in understanding the functional role of the cerebellum, which, until then, had remained obscure. It was, however, Luigi Rolando (1773–1831) who began a new era in cerebellar research by developing ablation experiments in an effort to understand the function of this brain area. Based on this work, he correctly suggested that the cerebellum is involved in motor control. Such ablation techniques, along with the subsequently developed stimulation methods, have served as basic experimental tools for understanding the cerebellar physiology for almost two centuries.

While this work was unfolding, clinical observations began to appear over a century ago, when it was realized that disorders exist in the human that cause a selective degeneration and atrophy of the cerebellum and profound
disturbances in motor coordination or ataxia. These disorders have provided a fertile ground for studying clinico-pathologic correlations in the human and have also generated further interest in basic cerebellar research. Because many of these disorders are genetically transmitted, they became known as hereditary cerebellar degenerations or ataxias. Due to the variety of their particular characteristics, these afflictions have attracted a considerable interest, particularly from the nosological point of view. It is, therefore, not surprising that the bulk of the bibliography accumulated over the past 120 years deals primarily with the clinical and pathologic descriptions and the much debated classification problem.

At the basic science level, rapid progress was achieved a few decades ago toward understanding the anatomy and physiology of the cerebellum following the description of the cerebellar cellular systems by Raymond y Cajal. The relatively simple architectural design of the cerebellum proved particularly suitable for understanding physiological processes at the neuronal and synaptic level. More recently, the introduction of new tools and experimental procedures, such as animal models, tissue-culture techniques, brain slices and subcellular fractions, immunocytochemical methods, chemical microanalysis techniques, molecular biology approaches, and neuroimaging applications have furthered our understanding of the cerebellum. Progress has also been made in recent years in the clinical sciences of the cerebellum. This field, no longer confined to the previously known descriptive level, is now progressing quickly, propelled by rapid advances in molecular biology, immunology, and neuroimaging.

2. THE CENTRAL THEME IN THE MODERN ERA OF CLINICAL CEREBELLAR SCIENCES

The central issue faced by the modern clinical neurosciences is the elucidation of the mechanisms involved in the basic phenomenon of neuronal degeneration, which is common to all human disorders with system atrophy. Identification of the factors that cause brain cells to die prematurely is a necessary prerequisite for understanding these disorders and for developing rational therapies. The basic neurosciences of the cerebellum are essential for understanding the fundamental properties of cerebellar systems and for providing insights into the factors that make these systems selectively susceptible to degeneration.

In line with these considerations, the main goal of this book is to bridge the basic with the clinical sciences for a comprehensive understanding of the cerebellum in health and disease. Bringing together the clinical with the experimental sciences could be of particular value for both the basic and clinical investigator whose work concerns the cerebellum. Thus, knowledge of advances taking place in basic sciences could help the clinical investigator to better understand the cerebellar mechanisms in order to develop new approaches and therapeutic strategies for these presently intractable human diseases. Also, the study of human disorders can provide basic investigators