
Preface

“The use of animals in medical research and safety testing is a vital part of the quest to improve human health. It always has been and probably always will be, despite the alternatives available. Indeed, in this era of genomics and proteomics, more rather than fewer animals will be needed. Without animal testing, there will be no new drugs for new or hard-to-treat diseases.”

Source: The Lancet. Vol 364 September 4, 2004

Traumatic brain injury (TBI) is a major and growing public health concern and a leading cause of mortality and morbidity worldwide, both in civilian life and on the battlefield worldwide. It is now considered as a complex spectrum of diseases associated with structural damage and functional deficits that are consequences of both primary and secondary injury mechanisms.

Most notably, over the past 50 years, TBI field has matured tremendously, and our understanding of the cellular and molecular biology along with the pathophysiological processes underlying acute and chronic TBI (and its recovery) has evolved. Throughout, this time research involving animal models of TBI has grown from a few individual laboratories to a global effort. Experimental TBI models have provided a driving force and undeniable contribution for much of this research allowing us to test hypotheses, to investigate basic mechanisms as well as to explore and determine the efficacy of novel potential treatments and therapeutic strategies. As a consequence, we have witnessed an explosion of “potentially useful” models replicating the various aspects of human TBI. However, it is now evident that to be effective in our quest for answers and cures, and to prevent failure in clinical translation of preclinical studies, methodological rigor, extensive standardization of outcome assessment, functional tests, pre-analytical and analytical aspects, and approach to treatment, as well as reproducibility are all essential.

The current volume represents an attempt to provide a list of the state-of-the-art currently established animal models of TBI thoroughly describing practical procedures, experimental methods, and protocols. While specific TBI models are discussed in different chapters, we view this as a strength because it exposes the reader to different viewpoints regarding model implementation and highlights the need for greater standardization in terms of reporting methods and findings. One noteworthy section of the book is dedicated to the *Combined Neurotrauma Models*—models combining a standardized TBI with systemic insults and multimodality monitoring—that can more adequately mimic the heterogeneity of clinical TBI.

As the experimental TBI research has grown, the diversity of outcomes continues to expand. The part on *Outcome Measures in Brain Injury Models* provides researchers with comprehensive methods of detecting behavioral, histopathological, cerebrovascular, imaging, and biochemical outcomes that aim at advancing the search for injury mechanisms and clinical translation.

This volume also aims to identify the issues and challenges related to TBI preclinical studies and offers guidance and solutions from renowned experts in this field that can certainly be of use for young investigators. We hope it can also be helpful to clinicians and laboratory researchers interested in the field and in fresh ways of addressing both experimental and clinical questions.

In this volume, we have assembled 40 chapters which have been authored by renowned experts in the areas of CNS neurotrauma and who are among the pioneers in the development of several of the currently used CNS injury models. The book opens with an introductory overview by Professor John Povlishock discussing the history and the evolution of experimental brain injury models. This volume is divided into six parts. Part II (General Consideration in Using Animal Laboratory in CNS Injury Research) describes general experimental concepts and approaches used in assessing CNS injuries, with emphasis on clinical and experimental models currently available and a summary of the development of these models along with a handy overview comparison of their different/respective characteristics. In the following part (Classical TBI Models and Their Link with Pathophysiological Features of CNS Injury—Models), the authors describe the utility of different injury models and their general pathological characteristics. This part elaborates on the different modified and novel experimental models ranging from pediatric rodent models of TBI to more recent models of diffuse axonal injuries. In Part IV (Special Topics in CNS Trauma: Comorbid Conditions in CNS Injury), we discuss the experimental combination of comorbid conditions in CNS injury models including hypoxia, hypoxemia, and epilepsy. In Part V (Outcome Measures in Brain Injury Models), assessment and outcome measures involved in CNS injury are systematically compiled to include a comprehensive summary of the behavioral and cognitive methods utilized. In addition, this part includes dedicated chapters discussing the utility of novel techniques and approaches that can be applied both in neurotherapeutics (stem cell therapy, small molecule inhibitors) and in evaluating indices in CNS injury models including proteomics, pressure myography, and mitochondrial bioenergetics. The volume closes with an overview chapter by Professor Frank Tortella who contributed a very nice piece discussing challenges that face preclinical models of TBI and translating them to clinical practice.

Finally, this book would not have been possible without the assistance of a large group of TBI experts, each of whom has particular expertise related to a given model. The contributing authors have done a superb job in presenting experimentally useful information and applied technical approaches of TBI-relevant models. We have also charged a set of investigators with the task of providing an overview of various aspects, current knowledge, advantages, and limitations of animal TBI models. Special gratitude goes to Professor Ralph Depalma who agreed to write the Foreword to this volume; his comments and suggestions have been always an excellent guide for researchers in the field of neurotrauma. We hope that the reader will find that these descriptions provide useful help and support as well as foster further innovation, development, and optimization of experimental TBI research.

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