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Vascular Mechanisms in CNS Trauma
Recognizing that the modern history of the study of traumatic brain and spinal cord injury has spanned less than 50 years, it is not surprising that our current understanding of the pathobiology and treatment of these devastating neurological disorders remains incomplete and in some cases, controversial. When first addressed in the early 1970s, the focus of neurotrauma research took a distinct vascular focus, with many believing that the most important mechanism underlying the morbidity associated with CNS injury was the occurrence of traumatically induced vasogenic edema. It was assumed that the mechanical forces of injury disrupted the blood–brain barrier leading to the extravasation of serum proteins and other damaging agents capable of recruiting increased water within the central nervous system thereby elevating intra-parenchymal/intracranial pressure. Further, it was assumed that this elevated pressure alone triggered all the damaging cascades of injury associated with tissue compression and subsequent CNS tissue damage. Others suggested that the same forces of injury altered vascular function leading to impaired autoregulation and/or impaired vasoreactivity to normal physiological challenges, predisposing the CNS to further injury when a secondary insult, such as hypoxia or hypotension ensued. This early vascular focus was solidified by the recognition that the same forces of injury, particularly those on the more severe end of the spectrum, invariably caused overt vascular damage reflected in local spinal cord hemorrhage followed by tissue cavitation or the occurrence of hemorrhagic contusional change within the cerebral cortex. In part, because of the failure of early clinical trials targeting vascular mechanisms to achieve therapeutic benefit and in part, due to the frustration of some over this vascular-dominated approach to neurotrauma research, the subsequent 2–3 decades of neurotrauma discovery took a decidedly neuronal centric focus. During this period, there was a dramatic shift in neurotrauma research to the considerations of altered neurotransmission/neuroexcitation, neuronal cell death framed in the context of apoptosis versus necrosis, axonal dysfunction and disconnection, and the sequelae of such disconnection in terms of CNS tissue deafferentation and neuroplastic change. These neuronal focused studies were interfaced with parallel metabolic, behavioral, and targeted therapeutic studies conducted both in animals and humans who had
sustained traumatic injury to either the brain or spinal cord. Unfortunately, as appreciated by all, this period of discovery, although highly significant, also failed to generate a full understanding of the pathobiology of CNS injury and/or lead to the development of more rational therapeutic approaches to improve outcome in those who have sustained traumatic injury to either the brain or spinal cord. In light of these limitations and clinical trial failures, the last decade has witnessed a more integrative approach, coupling the interaction of the CNS and its intrinsic vasculature, to better understand the overall pathogenesis of CNS injury and its potential therapeutic targeting. Now framed in the context of the neurovascular unit, contemporary research has begun to focus on the cell-specific responses therein while also exploring the various complex interactions between these neuronal vascular and their related glial pathways. In this context, renewed emphasis has been placed on the understanding of the blood–brain/blood-spinal cord barrier, not only in terms of its alteration following traumatic insult but also in the context of its ability to modulate nutrient transport as well as the passage of various purported neuroprotective agents.

Against this backdrop of discovery, the current text edited by Lo and colleagues frames our contemporary understanding of the vascular sequelae of traumatic injury to the CNS in an effort to achieve a more comprehensive understanding of CNS/neuronal responses to injury. The 29 chapters contained therein provide important insight into the complex and diverse vascular changes associated with traumatic CNS injury, with a good mix of both basic science and clinical discovery. The authors who have participated in the generation of this book provide detailed insight into virtually all of the important components of the vascular sequelae of injury and their CNS/neuronal interactions. The chapters in this text focus on important themes considering traumatically altered cerebral blood flow, autoregulation, vasoreactivity, coagulation, and blood–brain barrier status, while also addressing the importance of the neuronal/glial vascular unit. These studies are complemented by parallel considerations of more contemporary diagnostic and therapeutic approaches ranging from the use of proteomics and advanced imaging to the modern tools of electrophysiology and microdialysis-based assessment.

Collectively, the editors and authors are to be congratulated on their success in producing this important text. It will serve as an invaluable reference for those first entering the field as well as the seasoned investigator who wishes to update his or her understanding of the complex vascular sequelae associated with traumatic injury to the central nervous system.

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Preface

The vasculature of the central nervous system performs the vital tasks of perfusing the brain and spinal cord, and maintaining barrier functions that ensure a proper environment for neuronal activity. Additionally, the vasculature participates in other key functions, including the production of vasoconstricting and vasodilating substances, the provision of trophic support to the neuronal and glial parenchyma, the response to inflammatory stimuli, and the regulation of tissue remodeling and repair after injury. Hence, a rigorous understanding of vascular mechanisms is essential for the development of therapeutic strategies for brain and spinal cord trauma.

It is now an opportune time to incorporate the study of the vasculature in the field of CNS trauma science. Our hope in putting together this book is to provide a reference for clinicians and researchers who are undertaking further explorations of the CNS vasculature within the complex pathophysiology of injury and disease. We dedicate this book to investigators who are studying ways to treat patients and to improve the lives of survivors of brain and spinal cord trauma. And most importantly, we thank the many patients and families whose efforts to reclaim their lives after CNS trauma provide the inspiration for our work.

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