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Introduction

A Critical Problem Begging for New Insight and New Therapies

We dedicate this special issue of the *Journal of Neurotrauma* to the men and women of the United States military who have sacrificed their lives to defend our freedoms.

In this issue of the *Journal of Neurotrauma*, we are pleased to feature eight articles focused on the critical problem of blast-induced traumatic brain injury (TBI) and polytrauma. As a consequence of the Iraq war, blast injury has reached a new level of importance due to the high numbers of these types of injuries seen in our warfighters, and includes a wide spectrum of them, ranging from mild to severe. The pathobiology of blast-induced TBI remains poorly understood, and is complicated by many factors such as repetitive exposure and superimposed polytrauma. In the combat casualty setting, severe blast injury is a multi-system disease often involving extracerebral trauma, such as extremity injuries and burns. Blast injury is also emerging as a potential threat in civilian terrorism—such as that seen in the Madrid bombing in 2004—where combined insults such as blast-induced lung injury and TBI were observed (de Ceballos et al., 2005). We believe that the scope of articles in this issue appropriately reflects the multi-system nature of this condition in its most severe form.

We are pleased that a number of clinician-scientists and scientists working in this area have contributed either original articles or focused reviews. This issue also includes a comprehensive introductory overview on the topic by noted clinical experts Dr. Geoff Ling his and co-authors entitled "Explosive Blast Neurotrauma." Dr. Ling is the program officer overseeing the DARPA (Defense Advanced Research Projects Agency) PREVENT (Preventing Violent Explosive Neurotrauma) blast research program, which is focused on blast-induced TBI, and trying to shed light on some of the many mysteries that remain to be elucidated about this condition. Dr. Ling and his team provided neurosurgical and neurocritical care to our warfighters in Iraq, and thus impart in this review vital first-hand knowledge to the research community that reads *Journal of Neurotrauma* about this problem as it is currently being treated in theatre in Iraq (Ling et al., 2009). This should prove to be an extremely important article for those working in our field. We must link the field, the bedside, and the bench, if those of us in the neurotrauma research community are going to discover the answers to the many questions that remain in this field, and to help develop new therapies to treat this condition. The importance of this guiding principle is emphasized by Dr. Joseph Long and his colleagues at the Walter Reed Army Institute of Research in a report entitled "Blast Overpressure in Rats: Recreating a Battlefield Injury in the Laboratory," which shows that chest protection can be an important determinant of the severity of air-blast injury to the rat brain (Long et al., 2009).

We were also very pleased to receive manuscripts addressing a number of highly relevant topics to this condition, such as the seminal characterization of a model of blast-induced TBI in large animals by Dr. Richard Bauman and his colleagues in the PREVENT program titled "An Introductory Characterization of a Combat-Casualty-Care Relevant Swine Model of Closed Head Injury Resulting from Exposure to Explosive Blast" (Bauman et al., 2009). This group is currently carrying out critical studies of this problem by developing a unique model of munitions blast injury in swine, focusing on biomechanical, pathobiological, neuropathological, and neurologic consequences.

Dr. Svetlov and the group from Banyan Biomarkers, Inc., have provided us with an interesting report that addresses the important interface between experimental blast TBI models and biomarkers of brain injury that helps provide further insights into this field (Svetlov et al., 2009). We also received a related article by Dr. Denes Agoston and his group at the Uniformed Services University of the Health Sciences, that discusses proteomic applications in blast and non-blast TBI with a special focus on edema, inflammation, and neuronal death cascades (Agoston et al., 2009). Reviews are also included from Dr. YungChia Chen and colleagues on the utility of *in-vitro* systems to study blast-induced TBI (Chen et al., 2009), and from Drs. Douglas DeWitt and Donald Prough on experimental models of combined TBI plus secondary insults (DeWitt and Prough, 2009). These investigators are experts in their respective areas, and their articles address aspects of blast-induced TBI that are extremely relevant to those who work in our field. How to model blast injury *in vitro* is an important question, and polytrauma and secondary insults are so common in this condition that the neurotrauma research community must learn more about the impact of these insults, both on primary injury, and on the evolution of secondary damage (Okie, 2005; Gawande, 2004; Aschkenasy-Steuer et al., 2005; de Ceballos et al., 2005). Finally, here you will find a description of a new model of combined TBI and hemorrhagic shock in mice that will allow the future use of mutant mice in experiments to help examine some of the putative mechanisms of secondary damage, neuroprotection, and repair in these types of combined insults (Dennis et al., 2009), as heretofore such investigations

have largely focused on optimizing fluid resuscitation in large animal models.

There have been several recent reviews and seminal reports on blast-induced TBI that have addressed various aspects of this condition (Bhattacharjee, 2008; Hoge et al., 2008; Armonda et al., 2006; Okie, 2005; Gawande, 2004; Aschkenasy-Steuer et al., 2005; de Ceballos et al., 2005; Dennis and Kochanek, 2007), but many questions remain to be answered. For example, does blast-induced TBI differ from the spectrum of injuries seen in conventional civilian TBI? What experimental models of blast injury are best to study the human condition? Similarly, how accurately do our established TBI models such as controlled cortical impact or fluid percussion model blast-induced TBI in humans, and what are their shortcomings? What is the best way to test the different therapies for blast-induced TBI? What are the optimal approaches to mild versus severe blast-induced TBI, or single versus repetitive exposures? In this context, new knowledge about blast-induced TBI may allow us re-examine current treatments for conventional civilian TBI in a new light. For example, have we underestimated the role of vasospasm in conventional civilian TBI, based on the findings recently reported by Armonda and associates (2006) for blast-induced TBI? We believe the articles in this issue will help to build upon the seminal initial reports and reviews, and will provide new insights and stimulate new avenues of investigation into this crucial area of treating our warfighters, as well as the civilian population.

We also thank Drs. Claudia Robertson, Douglas DeWitt, Samuel Tisherman, and Hülya Bayir for the helpful suggestions they made during the preparation of this issue. Finally, I know that we speak for all of the authors whose work appears here in thanking Dr. John Povlishock, Editor-in-Chief, for giving us the opportunity to assemble this superb collection of articles for *Journal of Neurotrauma*.

Finally, in this issue, Dr. Povlishock has also included a special article on combination theraples for TBI authored by Drs. Susan Margulies, Ramona Hicks, and the Combination Theraples for TBI Workshop Leaders. This important article identifies key objectives and recommendations for the ultimate development of combination therapeutic approaches for TBI, a strategy that is likely to be critical to success in the many complexities addressing this condition.

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