# Research Frontiers in Traumatic Brain Injury

## Defining the Injury

Andrew J. Gardner, PhD[a,*], Shirley L. Shih, MD, MS[b], Elizabeth V. Adamov, DO[b], Ross D. Zafonte, DO[b,c]

**KEYWORDS**

• Research • Neuroimaging • Serum biomarkers • Blood biomarkers • Genetics • Physiology • Phenotypes

**KEY POINTS**

- Traumatic brain injury (TBI) is a dynamic field of research that has benefited from continued advancement in technology and ongoing developments across various scientific fields.
- TBI assessment, management, and prognosis has been improved through neuroimaging, biomarkers, genetics, and physiology studies.
- TBI premorbid risk, pathophysiology, and clinical phenotype are important considerations that influence clinical outcomes.

### INTRODUCTION

Traumatic brain injury (TBI) is a dynamic field of research that has exploded in the past decade. This increasing research interest has largely been associated with the continued advancement in technology (eg, neuroimaging) and ongoing developments across various scientific fields (eg, serum and blood biomarkers, genetics, and physiology), but also largely driven by the fact that TBI is a significant public health concern. It remains one of the leading causes of death among young adults and

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[a] Sports Concussion Program, Hunter New England Local Health District, Centre for Stroke and Brain Injury, School of Medicine and Public Health, University of Newcastle, University Drive, Callaghan, New South Wales 2308, Australia; [b] Department of Physical Medicine and Rehabilitation, Spaulding Rehabilitation Hospital, Harvard Medical School, 300 1st Avenue, Boston, MA 02129, USA; [c] Massachusetts General Hospital Home Base Program, Brigham and Women's Hospital, Massachusetts General Hospital, Red Sox Foundation, Boston, MA 02129, USA
* Corresponding author. Sports Concussion Program, Calvary Mater Hospital, Hunter New England Local Health District, Level 5 McAuley Building, Waratah, New South Wales 2298, Australia.
*E-mail address:* Andrew.Gardner@neurogard.com.au

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accounts for approximately one-half of all trauma-related fatalities globally.[1] The World Health Organization estimates that between 150 and 300 individuals per 100,000 are affected by TBI worldwide, of which around 10 million TBI-related hospitalizations or deaths occur annually.[1] In the United States alone, it is estimated that approximately 1.5 to 2 million Americans sustain a TBI annually. TBIs account for around 1.4 million emergency room visits, 275,000 hospital admissions, and 52,000 deaths in the United States each year. They contribute to approximately 30% of all deaths in the United States, annually.[2] TBI also has an enormous social and financial cost, with estimates of the annual financial burden associated with TBI ranging between $9 and $10 billion. TBI often results in residual symptoms that affect an individual's cognition, movement, sensation, and/or emotional functioning. Recovery and rehabilitation from TBI may require considerable resources and may take years.

Multidisciplinary approaches to TBI research have provided considerable insights into this injury, and epidemiologic studies have exposed the public health impact of TBI in relation to age, gender, and socioeconomic variables to incidence, prognosis, and outcome. In this special issue of *Physical Medicine and Rehabilitation Clinics of North America* on TBI, other articles have discussed fundamental issues such as the mechanism of injury, the biomechanics, pathophysiology, diagnosis, management, assessment/investigation(s), various postinjury sequelae, and potential long-term consequences. Therefore, the aim of this review is to provide an overview of the various new research approaches ("frontiers") that have been adopted around the world examining TBI, to discuss advancements in clinical trials, and to provide an overview of possible directions for future research. This discussion includes an overview of a range of TBI research, from sports concussion to severe TBI, from acute and subacute injury to long-term and chronic outcomes, from assessment and management to prognosis, specifically examining recent neuroimaging, biomarkers, genetics, and physiologic studies. The current review is less focused on discussing the underpinnings and background of the various technologies discussed (see other articles in this special issue for specific details) and more focused on the research findings and advancements in the TBI field. We also do not review potential novel treatment paradigms.

## NEUROIMAGING

Neuroimaging has been explored elsewhere in greater detail in this special issue (see Elisabeth Wilde 'Neuroimaging'). The increasing sophistication of advanced neuroimaging techniques has provided researchers (and clinicians) with an incredible insight, not only into the structure of the brain, but also into various aspects of its function (eg, connectivity, metabolism, blood flow, perfusion, magnetization transfer effect, and local field inhomogeneities).[3] Neuroimaging now has an increasingly important role in the clinical diagnosis and management of TBI. A number of advanced neuroimaging techniques that go beyond the capabilities of computed tomography (CT) and structural MRI have been increasingly used in TBI research. There are many variables that may affect the quality of data (the image resolution) that these techniques can acquire (ie, the magnetic field strength, the head coil specifications, improved filling of k-space), but also the processing of the data after acquisition. These processing techniques can sometimes rely on the manufacturer's automated software, but others are operator dependent, which means that the data can vary depending on the expertise of the operator. A number of these techniques and their capabilities have been outlined in a previous review.[3]