Chronic effects of neurotrauma consortium

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Mild traumatic brain injury (mTBI), also known as concussion, is a burgeoning epidemic in the US, with the CDC reporting that 1.6 million Americans sustain a TBI annually. Within the US military the number of TBI cases is increasing, with over 250,000 incidents between 2000–2012, the majority of which were mild injuries. While there is much debate over what classifies as a mild brain injury, the Department of Defense (DoD) defines a mTBI as head trauma associated with normal structural neuroimaging, with either (1) loss of consciousness for 30 minutes or less, (2) momentary alteration of consciousness lasting less than 24 hours or (3) post-traumatic amnesia also lasting for less than 24 hours. Clinically, mTBI is classified according to physical, cognitive and psychosocial functioning, that can include confusion, loss of consciousness, vestibular dysfunction, post-traumatic amnesia, headaches, sleep disturbance, depression and impaired cognition. Historically mTBI was thought to only be a temporary condition, although recent investigations have identified more prolonged symptoms such as post-concussive syndrome, as well as the possible development of chronic traumatic encephalopathy (CTE) decades after individuals are subjected to repetitive mTBIs. Thus, the term ‘mild’ injury may be misleading, referring only to the severity of the head impact and not the severity or time course of subsequent symptomology. While a mild injury causes ‘shearing’ or ‘tearing’ of long axonal projections in the brain, it is unclear how these injuries contribute to the large array of symptomology observed, such as those that occur immediately after the injury, right through to the development of chronic neurodegenerative diseases decades later. The risk factors that may lead to the development of these neurodegenerative diseases or other co-morbidities are also currently unknown.

Due to recent media attention on the possible association of mTBI with chronic neurodegenerative diseases, President Obama issued an Executive Order directing the DoD, Department of Veterans Affairs (VA), Health and Human Services and Education to develop a National Research Action Plan (NRAP) on TBI, with a view to improving agency co-ordination of research, leading to advances in the prevention, diagnosis and treatment of TBI. The NRAP identified challenges for TBI research and clinical care, including imprecise diagnostic tools and criteria used to classify the severity and type of TBI; a limited understanding of the impact of co-occurring conditions; gaps in understanding of mechanisms underlying injury and recovery, including the effects of gender, ethnicity and socioeconomic background; paucity of research data on the social, psychological and economic impacts of TBI on families and communities; uncertainty about the ability of pre-clinical models to reproduce the spectrum of injuries and co-occurring conditions; and a nascent understanding of ways to harness neuroplasticity to increase repair and recovery. Development of the NRAP led to the DoD and the VA jointly sponsoring the Chronic Effects of Neurotrauma Consortium (CENC), directed by Dr. David X. Cifu, MD, Chair of Physical Medicine and Rehabilitation at Virginia Commonwealth University, and Co-Directed by Colonel Sidney R. Hinds, MD, MC, US Army DVBIC National Director, and Dr. Rick Williams, PhD, from RTI International. The CENC is governed by a Government Steering Committee comprised of Government, DoD and VA subject matter experts, which approves all studies to be conducted, recommends new studies and identifies existing and new requirements as they arise.

The CENC is a co-ordinated, multi-centre collaboration, linking experienced basic science, translational and clinical neuroscience researchers from the VA, military and academia to address the long-term effects of mTBI and its diagnosis and treatment. To adhere to the NRAP guidelines on the challenges facing TBI research, the CENC created a roadmap that identifies knowledge gaps on mTBI pathophysiology and treatment. The CENC roadmap includes (1) understanding the incidence and pathophysiology of mTBI, (2) understanding whether mTBI pathophysiology is a risk factor in the development of neurodegeneration and other comorbidities, (3) developing diagnostic and prognostic tools for the pathophysiology of mTBI and (4) assessing the efficacy of interventions on mTBI pathophysiology. To begin to fill these knowledge gaps, the CENC currently has 10 research studies. As a dedicated co-ordinating centre, and to bring together each of the VA hospitals, one of the initiatives of the CENC was to create research cores to efficiently catalogue, track and manage the CENC patient samples, imaging data and neuropsychological data. These research cores encompass a Biorepository Core, a Neuroimaging Core, a Neuropathology Core, a Biostatistics Core and a Data Management and Study Management Core.

In short, the brain injuries incurred by US citizens and military service personnel are not well understood and there is limited knowledge regarding risk factors leading to physical, mental and emotional recovery of these individuals. It is hoped the CENC can provide a pathway to unravel the...
neuropathological basis and progression of mild TBI to expedite diagnosis, intervention and treatment programmes. The following articles in this special issue of *Brain Injury* provide an overview of the CENC research, including current preliminary data.

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