

Concussion within the Military

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Abstract

Concussion or mild traumatic brain injury (mTBI) is associated with long-term impairments in military personnel. Diagnosis of the condition remains clinically challenging. Neurological examination and cognitive symptoms may not accurately map the nature and severity of underlying brain injury. Neuroimaging techniques, such as diffusion tensor imaging (DTI), show promise as an effective tool in delineating the microstructural neural changes and corresponding clinical consequences following mTBI. This paper discusses the diagnosis and management of concussion, in the military context, using two cases of veterans who suffered blast-related mTBI. Insights on an integrated approach to concussion in the military, incorporating thorough neurological and neuropsychological examination and application of advanced neuroimaging are presented.

Key Words: Concussion, Military, Traumatic Brain Injury (TBI), Imaging, Simoa, Chronic traumatic encephalopathy (CTE)

Introduction

Concussion is a traumatic brain injury (TBI) which results in altered brain function¹. The expression thereof, is determined by the extent and region of the brain that is affected² and is amplified by repeated exposure to such insults. The effects are usually temporary³ but can include short-lived acute clinical symptoms that mostly resolve without intervention⁴. These symptoms may manifest as cognitive symptoms (impaired memory and concentration), affective symptoms (anxiety, depression, irritability, impulsivity, insomnia, ideation) and symptoms in the somatic domain (fatigue, headache, dizziness)⁵. Signs and symptoms of concussion may not appear until hours or days after the injury.

Blast-related mild traumatic brain injury (mTBI) has been called the 'signature injury' of the wars in Iraq and Afghanistan due to the significantly high prevalence in veterans previously deployed in these regions⁶. Over 300 000 United States (US) Armed Forces veterans have sustained a brain injury since 2003⁶. One in every 10 Australian Defence Force (ADF) personnel who have served in the Middle East reported post-concussive symptoms as per the criteria for a new mTBI^{5,6}. Repetitive mTBI is also a significant risk factor for neurodegenerative tauopathies including dementia and chronic traumatic encephalopathy (CTE)^{7,8}.

The US government has acknowledged the significance of concussion and established the Defense and Veterans Brain Injury Center (DVBIC), which is now part of the US Military Health System⁹. It is the TBI operational component of the Defense Centers of Excellence for Psychological Health and

Traumatic Brain Injury⁹. The mission of the DVBIC is to serve the active-duty military, the beneficiaries and veterans with TBI, adopting state-of-the-science clinical care, innovative clinical research initiatives and educational programs, and support for health protection of the target population¹⁰.

Post-traumatic stress disorder (PTSD) is an issue of major concern for the ADF and often overlaps with concussion and mTBI¹¹. In many cases, the cause of PTSD is ill-defined and requires further consideration¹². Symptoms of concussion and PTSD may overlap and be confused by those not linking the two¹³. Considerable research efforts, currently being undertaken in the US⁹, are modelled on a multidisciplinary approach to understand and address the effects of mTBI on military veterans returning from the overseas deployment. It considers the association of mTBI incidence, severity of post-concussive symptoms, comorbidities, social support, family functioning and community reintegration on long-term outcomes and the efficacy of rehabilitation interventions¹¹. Various treatment pathways targeted at mTBI in the military health system are also being studied, especially on veterans returning from Iraq and Afghanistan.

The cases that follow highlight both the needs and difficulties associated with the diagnosis and management of TBI. They identify areas of concern, new developments which may enhance diagnostic acumen and amplify issues for future research.

Case #1

A 35-year-old male soldier of Caucasian background was first seen in August 2017, and reported being

exposed to innumerable blasts while working with demolitions for the ADF. He reported at least 10 blast injuries while on deployment, being within 20–50 metres from explosions including an estimated 5 metres from an exploding projected grenade. He denied any loss of consciousness from any of these blasts.

In 2011, he reported being within 5–10 metres of a ‘controlled detonation’ of an explosive device, estimated to be equivalent to 5 kg of TNT, while inside the base compound. He reported feeling rattled but denied loss of consciousness. He described feeling shockwaves through his body when exposed to the explosion. In 2009, he reported firing a 66-mm rocket launcher, which he also described as a ‘shoulder-fired concussion weapon’, 60 times within a day, claiming 10 times per day is the upper limit. He had four deployments to the Middle East, all of which were associated with explosions and shockwaves. In addition, he reported five episodes of concussion while playing rugby.

On being examined during neurological consultation, he complained of 5 years of deteriorating memory. In 2013, he described an incident in which he failed to recognise his friend’s partner whom he had known for at least 2 years. He also reported a loss of memory of a fellow soldier with whom he had been deployed for 6 months. He identified problems with retrieving information unless that memory had been actively ‘jogged’. He claimed that newly acquired information was lost within 2 weeks if it was not repeatedly accessed and reinforced. He further reported difficulty retaining fine detail and specific information.

Using office administered clinical tools to evaluate cognitive function¹⁴, his scores were above average for the overall assessment, suggestive of no cerebral deficit. His remaining neurological examination was normal, as was standard brain imaging using magnetic resonance imaging (MRI) and electroencephalography (EEG). Advanced imaging including diffusion tensor imaging (DTI) was also performed to investigate the damage to the white matter tract.

He underwent detailed neuropsychological psychometric evaluation, which showed normal performance in the domains of: attention; concentration; processing speed; visuospatial processing; language; higher level skills; abstract reasoning; verbal fluency; planning; and problem-solving. Concurrently, psychometric testing demonstrated difficulties in: learning and memory measures; poor initial encoding for lengthy and

detailed verbal information; and mild reduction in learning recall of auditory information.

Case #2

A 39-year-old Caucasian male soldier was first assessed in July, 2016, stating that in 1999, while on deployment, he fell down a 100-metre ravine dressed in full battle rig and experienced loss of consciousness. He identified 1–2 hours of retrograde amnesia and 2 days of pro-grade amnesia. He was told that he walked out of the ravine and rejoined his patrol but he had no recall of this. He advised that he completed the exercise without further incident. In 2000, he presented and was treated for back symptoms, which he attributed to the fall but did not seek intervention for concussion.

Between 1998 and 2000, he stated that he undertook approximately 25 parachute jumps, in conjunction with his duties in the army. On two occasions, he reported a loss of consciousness in association with such jumps. He stated that they occurred in winds of more than 30 knots and reported loss of consciousness for 5–6 seconds before landing. He had no recall of grounding nor of 30 seconds to 1 minute after landing. He also stated that on one occasion he jumped at 700 feet, which was below safety standards and on impact claimed to have lost approximately 5 minutes. He did not report the incident.

Upon leaving the ADF in 2002, he joined the Police Force where he worked in riot control. He described an incident in which he was ‘king hit’, which resulted in 1–2 seconds of retrograde amnesia. He reported waking in the police sick bay approximately 5–10 minutes after the insult. He further reported numerous hits to the head between 2002 and 2005.

In 2005, he joined the US Department of Defense as a civilian contractor. He was deployed to the Middle East where he was exposed to an estimated 13 improvised explosive device blasts. He recorded four episodes of loss of consciousness and, while the incidents were reported to the authorities, he never sought medical attention in sick bay for consequences.

In 2006, he rejoined the ADF and experienced two episodes of loss of consciousness while playing rugby. He reported being sent off the field but returned to play within 30 minutes. The last of these incidents was in 2010.

In 2009, while serving with Special Forces, he reported being within 100 metres of an explosion which occurred behind him. He stated that the

blast was of such force as to blow him over. When he regained consciousness he was lying on his back, which he interpreted as the force being of sufficient intensity to both knock him down and roll him over.

His current complaints included: problems with anger control; episodes of altered consciousness, which he claimed to be epileptic seizures; gait disturbance with bradykinesia, freezing and bizarre movements; impaired cognition; sleep apnoea requiring continuous positive airway pressure (CPAP); and various tics and tremors.

Clinical examination revealed a very strange 'robotic-like' gait, which had features of psychiatric manifestations and was associated with slow movements, pill-rolling tremor and freezing. He had a speech disorder with stuttering and, at times, speech arrest. Testing higher-order cognitive function with in-house tools¹⁴ revealed impaired memory but did not identify any specific abnormality. Back examination was normal. Evidence of bradykinesia, pill-rolling tremor and lead-pipe rigidity were suggestive of extrapyramidal involvement with superimposing psychiatric features.

Standard imaging with MRI and a 48-hour sleep deprived EEG were both normal. In addition, he underwent advanced imaging including DTI. He responded well to anti-Parkinsonian medication including L-dopa, selegiline and pramipexole.

This case drew media attention as a special report on the Australian Broadcasting Commission (ABC) free-to-air television station. The presentation went to air with the approval and participation of the patient in August 2017¹⁵.

Discussion

Concussion remains the 'signature diagnosis' within military medicine, given its high prevalence in veterans especially with regards to the wars in Iraq and Afghanistan¹⁵⁻¹⁸, though TBI is gaining traction as a condition requiring additional research and understanding^{19,20}. It is essential to appreciate that, in the ADF, PTSD is acknowledged as of major importance¹² but the relationship between mTBI or concussion, and PTSD is not as well recognised.

Current management of concussion involves diagnosis, based on patient history and neurological evaluation in the clinic, exclusion of other pathologies, particularly structural head injury, for a differential diagnosis of concussion as well as careful consideration of potentially influencing factors²¹. Modifying factors that are crucial in mapping treatment plans include: current or future

engagement in high-risk activity or deployment; co- and pre-morbidity such as, migraine, depression and sleep disorders; use of psychoactive drugs; severity; sequelae (evidence of impact seizures or prolonged convulsive convulsions); and temporal features including frequency, timing and recency of concussions²¹.

The two cases presented in this paper, identify important features of TBI that deserve further consideration. Post-concussive symptoms are non-specific to mTBI/concussion. There is a large variability in severity, timeline and appearance of these symptoms, which make it diagnostically challenging. When combined as a 'cluster', these symptoms may be indicative of the condition. Given the nature of comorbidities, objective assessment of post-concussive symptoms is difficult^{16,22,23}, demonstrating a compelling need for further research to better understand the clinical implications of mTBI and to detect and quantify its prevalence and severity²⁴. In the two cases presented, DTI was able to capture alterations in white matter microstructural changes, even when the traditional diagnostic imaging modalities didn't find any abnormality.

Case #1 presented with repeated concussive episodes in whom office evaluation was normal, as were routine investigations. On more intensive formal neuropsychological psychometric assessment, he was shown to have defined areas of cognitive dysfunction. This emphasises the need to progress beyond routine clinical evaluation in patients with TBI who present as reliable witnesses and who offer a good history of ongoing problems. In most areas of psychometric testing, the patient scored within the average to above average range, thereby supporting the office evaluation. However, in specific tasks, there were confirmed areas of deficit requiring further attention.

Case #2 presented with repeated TBI in various situations in whom there were features of both neurological and psychiatric manifestations. Office evaluation confirmed problems with memory and physical examination showed evidence of extrapyramidal involvement with Parkinsonian features, which responded well to treatment and resulted in improved quality of life. There remained symptoms of a psychiatric nature which did not respond to such treatment and reinforced the concept that elements of both neurological and psychiatric manifestations can coexist in patients following TBI.

Further Considerations

It can be seen, from the above examples, that

routine clinical evaluation may be insufficient to adequately define the full nature and extent of the potential damage consequent to TBI. There is a need for further investigative tools of which there are a number of techniques, such as: enzyme-linked immunosorbent assay (ELISA); chemiluminescence; electrochemiluminescence; surface-enhanced Raman spectroscopy (SERS); induction coupled plasma mass spectrometry; immuno-PCR; and bio-barcode assay²⁵.

It has been argued that none of these are sufficiently robust to address recent experience of TBI and to consider the context of ongoing care²⁵. Advanced investigative techniques, such as single-molecule arrays with the simultaneous counting of singulated captured microbeads (Simoa™), a novel approach to determine peripheral concentrations of related compounds, may be of potential value in measuring concentrations of compounds such as tau, neurofilaments and Apo E protein in the peripheral blood and corresponding clinical consequences following mTBI²⁵. It is argued that Simoa™ uses an ultrasensitive sandwich array able to detect multiple micro-RNA's without pre-amplification and can detect these at femtomolar (fM) concentration ranging from 1–3 fM with high specificity²⁶. This technique may be of potential use to identify those who's TBI has probable negative prognostic values; however, for the present, it remains a tool in the research domain that warrants further investigation to determine its clinical value. It needs to be confirmed that Simoa™ will live up to expectation for reliability, validity and specificity, and that the correct peripheral compound is being appropriately measured in the right circumstances. Achieving this outcome will require ongoing studies and a commitment by all those involved. It represents a potentially exciting frontier, which may have wide application if the research supports the projected enthusiasm and expectation of its relevance.

A further consideration for investigation of TBI is reflected in more sophisticated imaging which is more sensitive in detecting alterations in neural micro-architecture. This may include DTI, which is a much more sensitive tool than conventional MRI^{8,24,27-30}. It must be acknowledged that both cases presented in this report were investigated with DTI but both initial reports, as provided by the radiologist, were 'normal'. This reflects the need for specialised and committed neurovascular, cerebral neuro-imaging skills to evaluate the relevance and applicability of DTI and the need to understand appropriate post-processing of the raw data to provide relevant diagnostic/radiologic results, especially in the military population who have experienced combat-related

blast/impact trauma^{23,24,27,29,31}. DTI pre-processing, post-processing, data visualisation, including tractography and radiological interpretation with clinical correlation, needs advanced, committed neuroimaging/neurovascular skills. Since advanced neuroimaging analyses is not routinely performed, customised platforms/programming are required to analyse DTI datasets.

A number of studies on veteran and civilian populations with mTBI/concussion indicate a role for advanced neuroimaging in objective assessment of brain injury from both diagnostic and prognostic standpoints, to better understand and predict neural and clinical consequences of the injury^{8,13,19,22-24,27-43}. It must also be acknowledged that there needs to be caution in extrapolating research, undertaken in a civilian population, to that in the military context, given the nature of source, complexity and wide heterogeneity of injuries⁵. Morphometric imaging studies, using T1-weighted, T2-weighted and fluid attenuated inversion recovery (FLAIR), have shown reduction in regional cortical thickness (as measured from the boundary of the white matter) in symptomatic military veterans who experienced mild- to moderate- TBI^{13,38,42}. Another promising imaging technique is diffusion weighted imaging (DWI), including DTI, that has been harnessed to study the neural microstructure in cases of concussion⁸. It is potentially more sensitive in detecting subtle effects of mTBI due to the axonal injury^{29,31,35}. Other studies have shown significant reductions in diffusion parameters, such as functional anisotropy (FA) values, as well as loss or variations in white matter integrity across several tracts in mTBI patients^{29-31,35,42}. Despite studies showing good sensitivity, future longitudinal studies are warranted to establish its diagnostic specificity and prognostic sensitivity before it is translated to routine clinical use.

Techniques of non-invasive measurement of regional brain metabolism, assessed as glucose uptake, measured using [¹⁸F]-fluorodeoxyglucose positron emission tomography (¹⁸F-FDG-PET) have also found significantly lower metabolism in the brain regions of the amygdala, parahippocampal gyrus and hippocampus in military veterans with history of blast-induced mTBI in comparison to the veterans without a history of blast exposure^{39,41,43}. ¹⁸F-FDG-PET can capture hypometabolism or compromised brain uptake of FDG for days to months after mTBI. This may be of value in clinical settings to stratify patients based on the stage of injury, type of injury and mechanism or to monitor the effects of medication for ongoing management of mTBI⁴⁴. Further studies (on a larger cohort) using ¹⁸F-FDG-PET, to study

the effects of trauma on metabolic activity in blast-induced mTBI war veterans, is required.

Other advanced emerging neuroimaging modalities, such as susceptibility weighted imaging (SWI)³⁷, arterial spin labelling (ASL)³², magnetoencephalography (MEG)²², electroencephalogram (EEG) phase synchronization⁴⁰ and spectroscopic imaging²⁴ have shown promise in studies of concussion-related brain injury. Their application has been limited in blast-induced mTBI in military populations. Advanced neuroimaging holds promise as a surrogate biomarker when combined with clinical and neuropsychological endpoints in early detection of mTBI, to characterise the nature and severity of injury. These techniques may assist in guiding therapeutic interventions, specifically in the context of concussion/mTBI in the military.

Amid concerns around the association of repetitive concussion/mTBI with CTE and dementia, further studies on clinicopathologic/radiologic correlation of the progression of the condition, following exposure to repeated concussion, is warranted^{7,45}. Large scale, multicentre, longitudinal studies on the effects of mTBI/concussion on veterans, using advanced imaging and monitoring techniques hold the potential to bring a paradigm shift in the care and treatment of affected individuals. It may also establish the clinical utility, sensitivity, specificity and accuracy of these techniques.

Conclusion

While TBI remains the 'signature' diagnosis for the ADF with the wars in Iraq and Afghanistan, it is insufficient to rely solely on bedside clinical skills. As with all neurological evaluation, history is the most important part of the assessment. If the subsequent clinical evaluation does not reflect expectation, based on the history provided, there is a need to progress to sophisticated investigation and potential use of

cutting-edge tools such as Simoa^{TM25} and advanced neuroimaging based characterisation of the nature and severity of the brain injury due to concussion/mTBI in the military^{22,28,31,32,38}. The cases provided reflect the lack of self-reporting of TBI by those who have experienced concussion/mTBI and this is most relevant to those within the Defence Forces where there exists a fear of the impact on a career path. As cutting-edge techniques develop and improve, there is an unequivocal need to properly subject those who have experienced TBI to further investigation, using an integrated approach²³. While there exists new and exciting technology, it is imperative to confirm the sensitivity, validity and reliability of such technology and to demonstrate that the correct test is being applied within the appropriate setting and is measuring the right variable(s). This necessitates an ongoing commitment to research in this field by people with the specialised and developed skills to demonstrate the benefit of these measures and their relevance to TBI and its clinical care.

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