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Accurate Assessment and Diagnosis for Traumatic Brain Injury

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Traumatic Brain Injury (TBI) has been described as the 'signature wound' of the conflicts in Iraq and Afghanistan with many sustaining brain injuries that exceed previous conflicts (Snell et al 2010). Brain injuries are invisible and/or initially may be overlooked due to priority being given to flesh/bone wounds or operational requirements.

Background

Traumatic brain injury is associated with significant morbidity and mortality both in military and civilian populations.

The incidence of mild TBI in those who have been in combat, with minimally impaired consciousness at the time of the injury, has been reported to be 3.2% and the prevalence has been reported to be 9.5% (Rona et al, 2012, Jones et al. 2014). In civilian populations NICE reported that the incidence is 0.47% with 1.4million people attending an emergency department each year. TBI is more common in those who have been involved in combat.

NICE report that 95% of people who have had a TBI have had a mild TBI and that the majority, >76%, recover without specific or specialist intervention. Yet others,

> "experience long-term disability or even die from the effects of complications that could potentially be minimised or avoided with early detection and appropriate treatment."
>
> (National Clinical Guidance Centre, 2020)

The majority of serious long-term problems and of those having fatal outcomes are in the moderate or severe head injury groups. None of the UK publications on TBI within the military report on the outcome in these groups.

As noted by a group at the King's Centre for Military Health and Academic Centre for Defence Mental Health, they were:

> "...unable to survey those who had been evacuated for further medical treatment, amongst whom the rate of mTBI with symptoms may have been higher"
>
> (Jones et al, 2014)

A further difference between the civilian population and those in the military is the observation that repeat injuries are much higher in the latter and exposure to high energy blasts is disproportionately higher in those who have been involved in combat. Repeat head injuries or exposure to sub-concussive blasts is known to be accompanied with Complex Post Traumatic Stress Disorder (C-PTSD) making diagnosis all the more difficult and are thought likely to be associated with a higher risk of neuro-degeneration or chronic traumatic encephalopathy.

The diagnosis of head injuries: a need for objective accurate testing

NICE guidelines are clear with respect to the diagnosis and management of those who have a putative head injury in the acute phase. They note that the main method of reaching a diagnosis is one of clinical judgement. In terms of objective measures used with that clinical judgement, CT scanning is the recommended imaging procedure.

In moderate and severe TBI, initial diagnosis is often made easier when the injury is mild. Unfortunately, CT and MRI scans in such mTBI patients often appear normal. Many groups, including NICE, have made statements concerning the need for improved, objective, means for assessing head injury and its longer term sequalae,

> "The availability of novel, objective methods of detecting brain injury provides an attractive means of better defining the presence of TBI in these contexts, with improvements in epidemiological precision. Perhaps more importantly, there is an increasing recognition that even mild TBI can result in prolonged cognitive and behavioural deficits, and the ability to identify patients at risk of these sequelae would aid clinical management, help determine which patients need novel therapeutic interventions, and refine resource allocation."
>
> (National Clinical Guidance Centre, 2020).

The consensus conclusion of a recent summit (Foss et al, 2020), supported by the Surgeon General, attended by UK Defence Medical Services, the Chair of the Independent Medical Expert Group (which advises on medical aspects of the Armed Forces Compensation Scheme), UK and US scientists, and clinicians from the UK and the US Department of Veterans' Affairs, included the following key recommendation that:

> "The military should employ pre-emptive medical assessment for those experiencing an event likely to have caused m/bTBI. This is rather than waiting for individuals to present later with symptoms. ....".

Crucially this consensus report came to the conclusion that:

> "**There is an urgent clinical need** to address the issues arising out of large numbers of military personnel and veterans with persistent symptoms of m/bTBI/PTSD....".
>
> (Foss et al 2020)

Imaging for head injuries

The Centre for Disease Control and Prevention in the US defines a TBI as "a disruption in the normal *function* of the brain that can be caused by a bump, blow or jolt to the head or penetrating head injury". Neither CT or MRI scanning can provide direct measures of brain activity and therefore function and the changes, if seen, using CT and MRI are late and reflect structural alterations in the brain.

In 1941, the UK Army led the world in showing that combat head injuries were associated with clear changes in brain activity and in particular they reported the presence of abnormal 'slow waves' in the electrical activity, the electroencephalogram (EEG) of the brain. Since

then, more than 800 scientific and clinical publications have confirmed and extended that initial significant finding.

In 1968 the ability to detect and isolate these abnormal slow waves took a huge leap forwards with the invention at MIT of powerful brain scanners that used quantum sensors to detect patterns of brain waves deep inside the brain. This technique called magnetoencephalography (MEG) has been employed to examine brain activity following head injury. MEG is a direct measure of a person's brain activity. It measures, non-invasively, magnetic fields around the head that were generated by the electrical activity of the brain. The advantage over the pre-existing EEG technology is that the signals were not blurred by the skull and skin and more precise measurements of brain activity and their sources within the brain could therefore be determined.

Importantly, MEG has been shown, repeatedly, to demonstrate abnormal activity following a head injury. In most cases these abnormal results resolve, and the patients returns to normal. However, as with the clinical symptoms, for a significant number, these changes persist.

MEG technology was subsequently adopted globally by over 136 academics and clinical centres (200 machines globally) and is used in many institutions across North America to assess military head injury. Importantly, the Department of Veterans' Affairs has published reports on the successful diagnosis of head injury using MEG in military personnel who have suffered blast and non-blast head injuries. Overall, more than 180 clinical and scientific articles have been published on the ability of MEG to be used to discriminate those who have had an injury from normal controls.

MEG is a very simple non-invasive procedure to use for measuring brain activity in TBI. Clinical investigations require a patient to lie in the scanner and just relax. These are called resting state scans and take about 30 minutes to carry out. The analysis of the recorded brain activity is then analysed using high performance computers and objective reports can then be generated on the statistical significance of the results, the location of the abnormality and changes that may have occurred since a previous scan and therefore can be used to monitor clinical progression to direct management and treatment.

A UK perspective on MEG scanning service provision and establishing a pathway for assessing military personnel and veterans

The UK are leaders in the science and use of MEG scanners. There are 10 such scanners in the UK. The MRC, Wellcome Trust and Wolfson Foundation have provided funding for these Centres.

Two of these scanners are routinely used for the assessment of patients with epilepsy and are installed in Centres that are inspected by CQC as they also provide clinical MRI services. All of the sites with MEG scanners were funded by the MRC to record brain activity in large cohorts from the normal population so that clinical cases could be compared against the results from those studies. In fact, the UK MEG community have established the largest database of what is normal brain activity.

A British company Innovision-IP Ltd provides patients and their referrers with independent objective reporting on TBI using MEG scans. Scans are carried out in Birmingham at a CQC registered Centre. Innovision has shown that it can use large datasets to report on whether a putative head injured individual has the brain activity signatures that distinguish such a person from the normal population and thereby accurately assess whether they have mTBI. One of the authors of this document (Professor Gary Green) is a founding director of this company and therefore declares a vested interest. He was a director and founder of the University of York Neuroimaging Centre which provides research and clinical services. He has now brought those 40 years of experience to that company with international counterparts leading the way in this field.

Within the UK there are extremely good links between the Defence Medical teams, the NHS, Veterans' charities, charities for the head injured, private companies providing support for Veterans and medical reports, as well as a number of international renowned research groups. These networks can be harnessed and further developed to provide a route from head injury assessment to management and treatment of head injured military personnel and veterans.

As with several other areas of best practice developed within the Defence Medical Services, as NICE have stated, addressing the issues of TBI in the military will have significant and far-reaching benefits for the UK population as a whole.

A pathway for the head injured personnel from the Defence Services

Many arguments have been made for yet more research to be undertaken before any attempt is made to implement a clinical service. This has led to delays in helping the injured, their families and done little to alleviate the impacts that head injury has on society including the documented increased presence of head injured individuals in prison. Delays have also increased the burden on social and mental health services, often as a result of misdiagnosis.

The recent documents calling for further research mentioned above fail to recognise the well-established and regulatory approval for procedures for acquiring MEG data from a scanner, their analysis and their interpretation for clinical use. Throughout the world there is regulatory approval for the use of MEG in a clinical setting. In the US FDA approval is in place for the use of MEG scanners to record brain activity and the American Medical Association have issued Current Procedural Terminology (CPT) codes for the use of MEG in clinical practice. Clinical adoption is not just in the USA but in many developed countries. In Europe MEG scanners are approved and used clinically to provide pre-surgical evaluation in 1000s of epilepsy cases. Across the world these scanners have CE approval for their safe use.

In the UK, MEG already provides a critical tool of diagnosis that provides a pathway to treatment.

Sir David Cooksey's report (Cooksey, 2006) highlighted that the pathway to clinical practice is not a simple case of a one-way push from the laboratory bench to the clinic but depends on clinical need and the constant interactions from many services along that pathway.

The opportunity and resources exist in the UK to use this approach to bring about real change for the military personnel, veterans and their families who are affected by the debilitating consequences of head injuries.

Conclusions

The Defence Select Committee Report(Part 2, P 40 – 108) states:

We recommend that the Ministry of Defence and the four UK health departments support further research work into mTBI including the testing of methods of clearly identifying this conditions".

" The government has a duty to not treat patients incorrectly as a result of misdiagnosis. In particular, Post Traumatic Stress Disorder (PTSD) and Mild Traumatic Brain Injury (mTBI) share some similar symptoms, which increases the risk of misdiagnosis of these conditions in serving personnel and veterans.

It is the request by the authors of this report that the Defence Select Committee recommendation above is taken forward and a funded pathway is provided for military

personnel and veterans suffering the long term symptoms of TBI be accurately assessed and diagnosed by the use of MEG.

Then this should provide the following immediate benefits:

1. The provision of objective proof of brain injury (where present) in military personnel and veterans, critical in cases where the presence of an injury has previously been overlooked, misdiagnosed or challenged.
2. The ability to link a particular combat event or events with a brain injury which can help the with the development of targeted preventative measures in combat and training going forwards.
3. A pathway to new treatments whose efficacy can be objectively monitored.
4. The establishment of a new database that can benefit the treatment of 1.3 million civilian patients suffering in the UK from long term symptoms of TBI would also benefit treatment.

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Appendix - 1

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136 Global Brain Centres using MEG - http://megcommunity.org/groups-jobs/groups

Innovision-IP Ltd – http://www.innovision-ip.co.uk

Appendix - 2

Articles on MEG and Head Injury

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