Shaken and Stirred –
Assessment of *mild* traumatic brain injury

“We see what we look for. We look for what we know”
Johann Wolfgang von Goethe

Introduction

The controversy surrounding the symptoms that follow seemingly mild traumatic brain injury is a long-standing issue, as this introductory story to an article from a law periodical makes clear:

“In a Supreme Court Trial several years ago, a medical expert was carefully explaining to the Judge the pathophysiological mechanism of traumatic brain injury. The Judge turned to the expert and remarked “the next thing you will be telling me is that you can have brain damage from a whiplash type injury”. The expert responded, well, yes you can. The Judge, obviously not impressed by this evidence, awarded the Plaintiff $20,000 in damages.”

The truth, however, is that the research in this area is high quality and well established:

“Researchers have clearly demonstrated that whiplash type, mechanical acceleration-deceleration injuries in primates produce observable brain damage. Rotational acceleration appears to be the primary mechanism responsible for the production of diffuse brain injuries. Similar brain damage has been observed in humans. Oppenheimer examined the brains of individuals who sustained minor to severe head injuries who died within several days of causes unrelated to the head injury. He found evidence of microscopic brain damage in cases where the cerebral injury was clinically trivial, consisting of a concussion which lasted for a few minutes. Oppenheimer concluded:

Following a head injury, diffuse microscopic lesions can be seen in the high proportion of human brains...They are believed to be mechanical in origin, and can be attributed to

1. surface sheering and contusions;
2. stretching and tearing of small blood vessels;
3. stretching and tearing of groups of nerve fibres;
4. tearing of nerve fibres by a crossing vessel

They can be seen, not only after severe trauma, but also in cases of ‘concussion’. Detailed studies of their sights and distribution could throw light on the mechanics of acceleration injuries of the brain”

From the 1960s and 1970s onwards, the relationship between what was considered mild traumatic brain injury and the potential for long term symptoms was recognised. The problem was not, therefore, that the facts were unclear; they were simply not well known. Education of the core messages remains an important element and the latest research in this arena adds more detail to those messages.

This article focuses on bringing our understanding of the shaken (neurological) element of the consequences of the injured brain up to date. The stirred (psychological) element is equally interesting but beyond the scope of this article.

The Pathophysiology of the Shaken Brain

The key mechanism underlying brain injury in the shaken brain is an acceleration/deceleration injury. The published data relating to this area conclude that the specific trigger for a traumatic brain injury which could lead to diffuse axonal injury (DAI) is a rapid onset, forward acceleration of the brain. The chance of such an injury causing significant DAI is exacerbated if there is any element of rotation. Understanding of the pathophysiology is increasing month by month; in November 2015 a new marker of axonal injury was defined.

The most complex element of this condition is in the inter-individual variation. On average the probability of a diffuse axonal injury is related to the change in velocity experienced. This is shown below in Figure 1:

![Figure 1](image-url)  

Figure 1: The relationship between cumulative frequency and change in velocity in DAI

The resulting injury creates a broad spectrum of tissue response within specific regions of the brain, some of which is physiological, some of which is permanent.

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5 Yoganandan, Gennarelli, Zhang, et al; J Trauma 2009
This combination of factors results in dynamic and patchy injury throughout the brain:

It therefore makes perfect sense that the latest evidence based review of this area concludes:

“It is important to assess individuals with post-concussion syndrome to try to determine the basis for the syndrome. This may make an important difference in treatment approaches and may be a factor in litigation of cases that involve post-concussion syndrome. The recommendations for assessment include use of an open-ended interview, a structured interview, use of a post-concussion syndrome questionnaire, interview of a third party who knows the individual being evaluated, thorough record review, psychological assessment, and neuropsychological testing with effort/validity assessment. An adequate assessment can help determine the psychogenesis or physiogenesis of post-concussion syndrome-type symptoms.”

The key to assessing patients with ‘mild’ traumatic brain injury is conducting a structured clinical interview focusing on discerning the important clinical features suggestive of DAI.
Immediate and Acute Symptoms

A structured assessment should take into consideration the following elements:

Loss of consciousness

While it is important to determine the presence and duration of loss of consciousness, it is equally vital to recognise that this is a poor guide to the presence of a mild traumatic brain injury. This has been established in animal models, which produce a pattern of DAI identical to human DAI and conclusively in the trauma and sports concussion literature, which is now the richest source of clinical evaluation of acute closed brain injury.

Neurogenic symptoms

A critical element of the assessment is to determine the presence or otherwise of ‘neurogenic’ symptoms as opposed to experiential symptoms. Recent studies addressing this issue have concluded that the following immediate and acute symptoms have a neurogenic basis:

- Headaches;
- Dizziness;
- Nausea;
- Intolerance of stress;
- Forgetfulness;
- Poor concentration;
- Taking longer to think;
- Blurred vision; and
- Personality change.

Trauma Related Amnesia

The presence and duration of post-traumatic amnesia (PTA) is an important feature, as the presence of PTA and the duration identifies those patients who are at a higher risk of developing permanent, significant subtle symptoms following their injury.

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Patients assessed and treated by the NHS are not routinely prospectively assessed for the presence of PTA using an appropriate tool. This is unfortunate, as when appropriate tools are used prospectively in patients with closed head injuries, significant PTA is often detected in patients with otherwise normal Glasgow Coma Scale (GCS) score, no overt evidence of confusion and normal brain imaging.

The pathophysiological correlation of PTA remains unclear; there are a variety of proposed mechanisms that explain why a patient can appear alert and lucid yet is still suffering PTA. It is also worth emphasising the extent to which the addition of a formal prospective assessment of post traumatic amnesia improves the sensitivity of detecting the presence of PTA beyond GCS and neurological assessment. The sensitivity increases from 13% to 60%. This implies significant PTA is frequently missed by the current systems of assessment in the NHS.

As PTA is a complex phenomenon accurate measurement, even prospectively, is challenging. The key element is the return of continuous memory. This amnesia has several specific, additional characteristics:

1. The nature of snapshots of memory: they are discreet, specific and associated with salient events;
2. The timing of snapshots: they all occur early in the PTA;
3. The state of the memory at the return of continuous memory: many patients are clear that although their memory is improved, it is of a significantly different quality to that of their memory prior to sustaining their head injury.

PTA typically has to be determined by retrospective analysis using a tool that has been proven to be valid for accurate retrospective assessment of PTA across a wide spectrum of head injuries. This is also the case if undertaken years after the original injury was sustained.

It should be noted that opiates can cloud a precise assessment of the aetiology of an amnesia following an accident and that in most studies considering this area patients who

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21 McCarter RJ, Walton NH, Moore C, Ward A, Nelson I., ‘PTA testing, the Westmead post traumatic amnesia scale and opiate analgesia: a cautionary note’
have consumed alcohol immediately prior to sustaining their brain injury are excluded. The studies of the impact of acute alcohol intake on memory per se suggest there are two types of black out in which amnesia occurs. The first, which is typically referred to as a black out, is where the person has no memory at all during the period that they are unable to recall. The second, and more frequent form, is termed a brown out, where the person does have partial recall and this can be very similar to PTA. Alcohol induced amnesia tends to be associated with rapid drinking rather than high volume consumption and the onset is typically gradual rather than sudden and obviously temporally related to the rapid ingestion of alcohol. Alcohol induced amnesia typically recovers rapidly and completely after a period of sleep.

Usually retrograde amnesia is either not present or is significantly shorter than anterograde amnesia in patients who have sustained a mild traumatic brain injury. When present, acute retrograde amnesia is directly related to the duration of anterograde amnesia, as demonstrated in Figure 4 below:

![Figure 4: The relationship between the duration of anterograde amnesia and the severity of retrograde amnesia](image)

In less than 1% of patients, a complex retrograde amnesia, which can date back many years, is present. This type of amnesia is consistent with those described in articles describing retrograde amnesia associated with other organic causes. I have noticed the presence of this type of retrograde amnesia is typically assumed by many experts to be more consistent with a somatoform disorder. Despite doing an ‘acute neurological take’ where I saw many patients with “minor” head injury over a 15 year period (in Sydney, Sheffield and Plymouth), and having an active interest in medically unexplained symptoms, I can not recall ever

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seeing a case of ‘psychogenic amnesia’ triggered by a head injury. I have however, seen complex retrograde amnesia in about 5% of patients. I have seen cases of amnesia associated with presumed ‘dissociation’ but the amnesia in these cases was a minor feature of the patient’s clinical syndrome compared to the motor symptoms, the amnesia was a total blank and was short lived compared to motor symptoms.

The published literature in the area of ‘psychogenic amnesia’ helps to clarify the nature of this amnesia:

“FUNCTIONAL AMNESIA AND ITS TYPES

The memory impairment in ‘functional amnesia’ is usually of a retrograde nature, but might at times be anterograde as well. Although impaired recall of autobiographical events is the most prominent symptom in psychogenic amnesia, deficits in retrieving personal facts and general semantic (non-personal) knowledge can also occur. In addition, variable degrees of anterograde memory deficits (as detected by standard anterograde memory tests) can accompany the retro-grade amnesia. However, in most patients with functional amnesia, anterograde mnemonic processing was reported to be preserved to a large extent (my emphasis).

Presence of Overlap Injuries

Structured inquiry relating to traumatic damage to other structures (hearing, vestibular, facial) in the skull often reveals symptoms which might otherwise be missed. Their presence also helps illustrate the severity of the acceleration-deceleration injury that has been suffered.

Sub-acute and Chronic Symptoms

Post-traumatic headache

Post-traumatic headaches are extremely common. A recent paper revealed that:

- 18% of patients reported having a problem with headaches pre-injury;
- 54% reported new or worse headaches compared to pre-injury immediately after injury;
- 62% reported new or worse headaches at three months, 69% at six months, and 58% (109/189) at one year.

The authors concluded that:

“Headache after mTBI is very common and persistent across the first year after injury. Assertive, early treatment may be warranted to avoid chronicity and disability. Further research is needed to determine whether post-traumatic headache (PTH) responds to headache treatment used in the primary headache disorders and whether chronic PTH is preventable.”

**Long-standing Symptoms**

The following symptoms are consistently associated with the presence of DAI:

- Fatigue;
- Sleep disturbance;
- Intolerance to noise;
- Intolerance to alcohol;
- Reduced libido;
- Marked symptoms that the patients are unaware of but that others have commented upon;
- A significant change in personality,
- Problems with working memory;
- Problems with decision-making;
- Difficulties with problem solving;
- Problems with multi-tasking;
- Problems with concentration;
- Problems with social monitoring;
- Problems with social control;
- Problems with intuition;
- Difficulties with new learning; and
- Word finding difficulties.

The correlation between the chronic physical and cognitive symptoms and diffuse axonal injury (DAI) is well established, as outlined in Figure 5 below. This also demonstrates that the symptoms map to specific regions of the brain and that having DAI does not necessarily mean that a patient will exhibit all of the symptoms that are associated with this injury.

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The Role of Imaging in the Diagnosis of Diffuse Axonal Injury

One of the most misunderstood areas of this condition is that ‘normal’ CT scan and 3T MRI scans are consistent with the presence of DAI. The published literature has shown that attempts to correlate visible lesions on any currently available routine imaging modality to clinical symptoms in patients with DAI have proved disappointing. The explanation offered in the literature is that the clinical deficits relate to a “more general compromise of the integrity of underlying white matter, which may connect topographically distinct regions”32. This review of the utility of conventional imaging in patients with DAI states:

“Historically, the widely distributed, microscopic nature of the axonal pathology in DAI rendered it essentially invisible with conventional brain imaging. As such, DAI was often a “diagnosis of exclusion” for patients with persisting symptoms related to head injury, but no radiological findings. In some patients, minor changes in the white matter have been found with conventional imaging techniques but likely reflected associated pathologies, such as microbleeds rather than actual axonal pathology”33.

New imaging modalities

There are new imaging modalities emerging, which are reviewed in a recent article34. The most clinically relevant of these is susceptibility weighted imaging (SWI), which can reveal

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strategically placed micro-haemorrhages that are highly correlated with the presence of diffuse axonal injury. However, the most recent review of the utility of this sequence in patients with head injury stresses that this only increases the tip of the ‘diffuse axonal injury iceberg’; currently, SWI is calculated to have a sensitivity of 23% and a specificity of 89%\textsuperscript{35}. Therefore, normal imaging does not exclude a diagnosis of diffuse axonal injury.

**Post-traumatic epilepsy and post-traumatic dementia**

Traumatic brain injury leads to an increased risk of developing post-traumatic epilepsy and post-traumatic dementia. For both conditions, the level of risk is determined by the classification of the severity of the traumatic brain injury. The level of risk can often be underestimated as a result of superficial assessment of PTA; this aspect is critical, because the duration of the PTA is a determining factor in the classification of the severity of the brain injury, i.e. a patient who is assessed as having a mild brain injury on the basis of all other factors (e.g. imaging, loss of consciousness etc.) may be re-classified as having a moderate or severe brain injury as a result of the nature of the PTA they suffer.

**Post-traumatic epilepsy**

The increased risk of developing post-traumatic epilepsy is shown in Figure 6 below:

![Cumulative probability of late unprovoked seizures after traumatic brain injury (TBI) in seven studies.](image-url)

Figure 6: Cumulative probability of late unprovoked seizures after TBI in seven studies

Post-traumatic dementia

Post-traumatic dementia (PTD) is an emerging issue. A paper by Srivli et al, entitled *Dementia resulting from traumatic brain injury, what is the pathology?*, published in the Archives of Neurology in October 2012, is a comprehensive review of the state of play with respect to the relationship between traumatic brain injury, both as a single event and as a chronic phenomenon, and the development of dementia. The paper contains the following statements:

“...traumatic brain injury is perhaps the best established environmental risk factor of dementia”.

“On the basis of these and other studies, an Institute of Medicine committee concluded that “there is sufficient evidence of an association between moderate and severe TBI and dementia...limited suggestive evidence of an association between mild TBI (with loss of consciousness and dementia) and inadequate insufficient evidence to determine whether an association exists between mild TBI without loss of consciousness and dementia”.

Since this time there have been further publications in this area. The first paper is entitled *Dementia risk after traumatic brain injury and non brain trauma, the role of age and severity* (Gardener et al). This was a retrospective cohort study, which was performed from 2005 to December 2013, all patients 55 or older diagnosed as having TBI or non TBI trauma and who did not have a baseline dementia or die in hospital were included. The study included 164,661 patients in the California state wide administrative health database of emergency department and inpatient visits. Patients were coded as having mild versus moderate to severe TBI.

The results showed a total of 51,799 patients with trauma, 31.5% with TBI. Of these 4,364 (8.4%) developed dementia compared with 6,610 patients with non traumatic trauma (5.9%) p<0.001. In younger patients the risk was associated only with moderate or severe TBI, in patients over 65 all severities of TBI were associated with increased risk of dementia.

These findings add further support to existing positions in the published literature with respect to dementia risk following TBI. This paper also helps clarify an additional point. There is a growing body of literature that reveals that the temporal pattern of the cognitive decline is progressive.  

![](https://example.com/figure7.png)

Figure 7: Model of premature brain ageing in traumatic brain injury

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Figure 8 below, taken from the Gardener et al paper described above, clearly shows a pattern consistent with the ‘interactive effects trajectory’ in Figure 7.

Further evidence for this pattern of progression comes from a very recent paper. This paper accessed the extent of brain atrophy following TBI. The findings were clear; atrophy is accelerated following TBI, this correlates with clinical symptoms and this atrophy accelerates over time (see Figure 9).

Figure 9: Grey matter and white matter predicted age difference (PAD) score increases with greater time since injury (TSI)

Conclusion

For a patient to develop DAI following a traumatic brain injury is a devastating life event. In my clinical practice I have found the presentation of these patients very stereotypical and consistent. It is also clear that the patients struggle to make sense of their symptoms themselves, as do their family and friends and treating clinicians; this often exacerbates the problems that these patients are experiencing. For a medico-legal process to then compound this problem feels like the final insult. Goethe said: “We see what we look for. We look for what we know”. In the case of DAI following traumatic brain injury it is time to acknowledge that this is a known problem, with a weight of evidence to describe its effects and presentation, and to ensure that the medico-legal assessment of patients takes place with that truth in mind.

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