Review

VISUAL PROBLEMS ASSOCIATED WITH TRAUMATIC BRAIN INJURY

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Abstract

Traumatic brain injury (TBI) and its associated concussion are major causes of disability and death. All ages can be affected but children, young adults, and the elderly are particularly susceptible. A decline in mortality has resulted in many more individuals living with a disability caused by TBI including those affecting vision. This review describes: (1) the major clinical and pathological features of TBI, (2) the visual signs and symptoms associated with the disorder, and (3) discusses the assessment of quality of life (QOL) and visual rehabilitation of the patient. Defects in primary vision such as visual acuity (VA) and visual fields, eye movement including vergence, saccadic and smooth pursuit movements, and in more complex aspects of vision involving visual perception, motion vision ('akinopsia'), and visuo-spatial function have all been reported in TBI. Eye movement dysfunction may be an early sign of TBI. Hence, TBI can result in a variety of visual problems, many patients exhibiting multiple visual defects in combination with a decline in overall health. Patients with chronic dysfunction following TBI may require occupational, vestibular, cognitive, and other forms of physical therapy. Such patients may also benefit from visual rehabilitation including reading-related oculomotor training and the prescribing of spectacles with a variety of tints and prism combinations.

Key words: Traumatic brain injury (TBI), Visual signs and symptoms, Visual fields, Eye movement, Ocular rehabilitation

Introduction

Traumatic brain injury (TBI) results when an external force injures the brain and is a major cause of death and disability. All ages can be affected but children, young adults, and the elderly are especially vulnerable.[1] TBI has many causes including falls, vehicle accidents, violence, sporting activity, and as a result of military action in war zones. TBI is also potentially associated with large per capita direct and indirect costs because of the frequently young ages involved and the severity of subsequent disabilities.[2] Relatively little has been published on the economic burden of TBI[3] but estimates suggest in the USA $81 million in direct costs and $2.3 billion in indirect costs in a single year from the non-use of bicycle helmets alone.[4]

A frequent result of TBI is concussion caused by the rapid acceleration of the brain so that it impacts the inner walls of the skull which can cause both focal lesions such as cerebral laceration and hemorrhage and more diffuse damage resulting in edema and axonal injury.[5] Most fatalities from TBI occur within days or weeks following the traumatic incident[8] with approximately 40% of cases deteriorating after hospitalization.[7] Damage caused at the moment of injury can also have secondary effects including damage to the blood brain barrier and white matter fiber tracts.[6] TBI can also cause physical, cognitive, social, emotional, and behavioral effects and prognosis can be unpredictable varying from complete recovery to permanent disability or death. Recently, there has been an overall decline in mortality due to TBI as a result of improved treatment, but as a consequence, an increase in individuals living with a disability as a direct result of TBI.[9]

TBI can result in a variety of visual problems affecting both the afferent and efferent visual system.[10] In particular, patients with a less severe form of TBI can exhibit visual consequences which are prolonged and are the most likely to be seen by eye practitioners. This review describes: (1) the general features of TBI including prevalence, classification, signs and symptoms, and pathology, (2) the visual signs and symptoms associated with TBI, and (3) the assessment of quality of life (QOL) and visual rehabilitation of the patient. The various terms that have been used to describe and classify the condition and its consequences are listed in Table 1.

General features

Incidence and Prevalence

Recent estimates in the USA suggest 235 000 citizens are hospitalized each year with non-fatal TBI, 1.1 million visit emergency departments, and approximately 50 000 patients die from their injuries.[11] In addition, a rate of residual disability of 43.3% has been recorded one year after injury. In studies conducted in the USA, Europe, Australia, and New Zealand, 691/100 000 children and young adults with TBI were treated in emergency units and 74/100 000 in hospitals, the subsequent death rate being 9/100 000.[1] Longer-term disability was estimated to be approximately 20% in those patients that were hospitalized. Males were more at risk than females and falls were the major cause in children and motor vehicle accidents in young adults. In Europe, in the period 1990-2014, overall incidence of TBI was 262/100 000, reaching a peak in older age groups, falls being the most common cause.[12] Furthermore, in European studies carried out in the period 1980-2003 comprising 23 separate reports, aggregated hospitalized and fatal TBI was estimated to be 235/100 000 and average mortality to be 15/100 000, the ratio of mild to moderate to severe cases being 22:1.1:1 suggesting a large group of mildly-affected individuals living with the consequences of TBI.[13] A further study carried out in the USA confirmed these conclusions and estimated 1.1% (3.17 million) civilian US citizens were living with long-term disability associated with TBI in 2005.[14] Variation in incidence and causation over time has also been reported. In an Italian study carried out in the periods 1997-1999 and 2006-2008, incidence of TBI was 2019 and 1232 per year respectively[15], that attributable to falls increasing over the period but declining due to vehicle accidents. An unusually high incidence of TBI of unknown cause, viz. 24.9/10 000, has been reported in northern Sweden.[16]

Headache is the most common and persistent symptom following TBI.[17] In a study of 212 TBI patients, 18% had reported headaches pre-injury but 54% reported new or enhanced headache post-injury, one week after trauma.[18] In addition, the cumulative incidence of headache was 91% over one year while 49% of patients met the criteria for migraine or probable migraine, and more than 40% for tension-type headache.[18] The prevalence of post-traumatic stress disorder (PTSD) has been estimated to be

18% following a TBI, the degree of severity being influenced by gender, longer loss of consciousness, and whether the injury was inflicted intentionally.[19] There is also considerable current interest in whether TBI is a risk factor in the development of dementia later in life associated with Alzheimer's disease (AD)[20] or chronic traumatic encephalopathy (CTE)[21,22] largely associated with concussion in sport.[23] Hence, in Taiwan, a previous incident of mild TBI gave a hazard ratio (HR) of 3.26 of developing dementia in later life.[24]

With reference to visual dysfunction, in one of the earliest studies of 254 TBI patients discharged from a comprehensive rehabilitation program, visual difficulties, headache, and fatigue were observed in a significant number of patients.[25] In 100 subjects 11-17 years of age with concussion, 69% had at least one visual problem, most commonly affecting accommodation, convergence, or saccadic and smooth pursuit movements.[26] In addition, in a population of hospital inpatients with TBI, approximately 60% were impaired in one or more visual functions involving eye movement, stereopsis, and near/far eso-exotropia.[27] Approximately 65% of military personnel with TBI as a result of blast injury reported visual problems.[28] In a further study of blast-induced injury, 68% of patients (N = 21) had visual problems, most commonly photophobia, difficulties in reading and convergence and accommodative insufficiency.[29] In pediatric patients with concussion, 13% of 275 patients had persistent near point convergence abnormalities which were referred for vision therapy.[30]

Classification of TBI

TBI can be classified according to severity, causal mechanism, or location of injury. Severity is usually assessed as mild, moderate, or severe using the Glasgow Coma Scale (GCS), a 15-point scale based on measures of verbal, motor, and eye-opening reactions to various stimuli.[31] A score of 13 or greater is regarded as mild, 9 - 12 moderate, and 8 or below severe. The US Department of Veterans Affairs uses GCS in combination with duration of post-traumatic amnesia (PTA), loss of consciousness, and neuroimaging findings such as swelling, focal lesions, or diffuse injury to assess their patients.[32] There are also grading scales to assess mild TBI which use duration of loss of consciousness, PTA, and other symptoms.[33]

TBI can also be classified according to causal mechanism. Acquired brain injury (ABI) is a general descriptive term and such patients can be divided into two groups depending on whether a traumatic or non-traumatic cause, such as stroke or infection, is involved. If a traumatic cause is present, this may be due to an impact to the head, blast injury, or penetration by a projectile, the resultant damage being focal, diffuse, or not easily detectable.[34]

Signs and symptoms

Moderate to severe TBI is often associated with a range of clinical symptoms including persistent headache, nausea/vomiting, convulsions, inability to awaken, dilation of one or both pupils, slurred speech, aphasia, dysarthria, weakness/numbness of limbs, loss of coordination, restlessness, and agitation.[17] Longer-term changes in such cases can affect social behavior, cause poor judgment, and result in cognitive changes affecting speech and executive function. Patients with mild TBI may exhibit many of the same symptoms but to a lesser degree with in addition balance problems, blurred vision, tired eyes, tinnitus, fatigue, and sleep disruption. All patients may experience cognitive and emotional changes which affect behavior, mood, confusion, and memory.[17] In addition, a variety of visual symptoms are present to be discussed including visual acuity (VA) and visual fields, eye movement including vergence, saccadic and smooth pursuit movements, and in more complex aspects of vision involving visual perception, motion vision (’akinopsia’), and visuo-spatial function and will be discussed in more detail below.

A concern is whether the long term effects of TBI can result in neurodegenerative brain disease. In particular, CTE is a dementia believed to result specifically from repeated incidents of TBI.[35,36] It has been recorded in association with a variety of contact sports such as boxing, American football, hockey, and wrestling[37] and has also been reported in military veterans exposed to blast shock waves from explosive devices.[21,22,38,39] Although controversial[40,41], a history of TBI appears to be the only risk factor consistently associated with CTE.[37] The clinical symptoms of CTE include impairment of memory and executive function, behavioral change, and the presence of motor symptoms.[42] As a consequence, TBI may be associated with clinical

symptoms, including those affecting vision, many years after a traumatic incident and can affect all aspects of professional, social, and family life.

Pathology

The specific symptoms of TBI usually depend on whether an injury occurs within the skull but outside the brain (extra-axial) or within the brain (intra-axial), whether the injury is diffuse or focal, and the specific brain regions affected.[34] Diffusion tensor imaging (DTI), a technique in which images are created to reflect various different properties of a tissue, has been particularly useful in revealing damage to white matter fiber tracts.[43] Most focal injuries affect the orbito-frontal cortex (Brodmann's areas BA 10,11) and the anterior temporal lobe (BA 38), regions involved in the regulation of emotion, olfaction, and decision-making. Cerebral laceration, i.e., if the tissue is cut or torn, commonly affect the orbito-frontal cortex because of the presence of bony protrusions on the internal skull ridge above the eyes.[44] In addition, hemiparesis or aphasia can occur when motor or language areas are damaged but these injuries are less frequent. Focal collections of blood resulting from brain hematoma can also occur.[45] By contrast, a diffuse injury may not be apparent even on neuroimaging and only detectable after histological studies.

Deterioration after hospitalization with TBI usually results from secondary injuries caused by cellular degeneration and the initiation of biochemical 'cascades'.[8] These injuries result from damage to the blood brain barrier, the release of inflammatory factors, formation of free-radicals, cytotoxicity due to the release of the excitatory neurotransmitter glutamate, the influx of calcium and sodium ions into neurons, and mitochondrial dysfunction.[8] Secondary injury can also cause white matter axons to separate from their cell bodies leading to cell enlargement and loss of neurons.[8,46] Changes in blood flow may also lead to ischaemia, cerebral hypoxia, oedema, and raised intracranial pressure (ICP).[8]

A variety of pathologies may be associated with CTE including reduced gray matter volume, most prominently affecting the frontal and anterior temporal lobes, together with enlargement of the lateral and third ventricles.[21,47] A molecular pathology is also present in which the major constituent is the microtubule-associated protein (MAP)

tau. This tau-immunoreactive pathology varies from the presence of neurofibrillary tangles (NFT) within the cytoplasm of neurons in frontal cortex[48] to a more widespread and severe pathology affecting the temporal lobe, limbic system, and the striato-nigral system.[28] CTE is also frequently associated with AD pathology, viz., extracellular deposits of beta-amyloid (Aβ) resulting in senile plaques (SP).[49-51]

Visual problems in TBI

The visual problems reported in TBI are summarized in Table 2. Aspects of visual function have been divided into various categories based largely on those used to characterize vision in the dementias.[20] Although these aspects of vision are discussed individually, many patients exhibit multiple visual defects.[26,27]

Visual acuity (VA)

Poor visual acuity (VA) can significantly affect many aspects of a patient's QOL. Studies suggest a significant loss of visual acuity (VA) in some patients with TBI, which can impair performance both at work and in sport. In major league baseball in the USA, a concussion will often impair balance, VA, and reaction times resulting in significantly reduced batting performance.[52] In addition, a large sample of military personnel was studied with combat injuries comprising 68 inpatients with moderate to severe TBI, all in rehabilitation, and 124 outpatients with mild TBI. The majority (78-98%) had a VA of 20/60 or better. However, inpatients and outpatients experienced a VA loss ranging from 20/100 to no light perception in 13% and 1.6% of individuals respectively.[53] VA deficits in TBI can also be persistent, a patient with impaired VA and cortical blindness after an injury still experienced poor vision a year later.[54] Blast-exposed veterans with poor VA may also experience significantly poorer visual QOL.[55]

Photophobia

Intermittent and chronic photophobia has been reported in TBI attributable to the injury and co-morbidity associated with migraine and can affect QOL.[29,56] Light-

filtering lenses may be useful in limiting the symptoms but to date, but more studies are needed to support this observation.[57]

Colour vision

Few studies of colour vision have been carried out in TBI patients and this aspect of vision requires further investigation. Nevertheless, a study of primary colour discrimination of 11 TBI patients and 11 controls using a primary colour discrimination task and event-related potentials (ERP) has suggested deficits in colour vision may be present in TBI although a specific colour deficit was not detected.[58]

Stereopsis

Stereopsis or depth perception is needed for many common visual functions including driving, climbing stairs, and reaching out to take hold of an object. In a population of hospitalized patients with TBI, a significant proportion exhibited defects in stereopsis.[27] In addition, in a study of 10 mild TBI patients with poor depth perception, perceived distance stereo-acuity was measured at 40 cm and 3 m.[59] No significant differences were detected when compared with control patients at any distance, mean distance responses under monocular and binocular viewing conditions being similar. Hence, depth perception problems in TBI may not be a binocular vision problem but a consequence of 'higher-level' dysfunction related to diffuse cortical injury.[59]

Visual fields

Visual field loss can be a significant factor in the ability of person with TBI to sustain subsequent employment. Mild TBI can be associated with damage to the optic radiation including a loss of tissue volume affecting one or both sides of the brain.[60] In addition, axons traversing the corpus callosum are vulnerable in TBI.[61] In a study of 14 mild TBI and 14 controls, inter-hemispheric propagation was affected more commonly in the patient group, transmission failure measured using the 'travelling wave' method in which two different stimuli are presented to each eye being

topographically distributed with a bias towards greater failure affecting the upper visual field.[62]

As a consequence of this pathology, a number of studies have reported visual field problems in TBI.[10,28,55,62,63] Of 880 patients with homonymous hemianopia studied in 1989-2006, 103 were associated with TBI largely as a result of a vehicle accident, the sample including 39% of patients with a complete and 61% with an incomplete hemianopia.[64] Occipital lobe damage was present in 13% of these patients while optic radiation and optic tract lesions were observed in 23% and 11% of patients respectively, lesions being present at multiple sites in 54% of patients. Other types of field defect have also been reported in TBI including bitemporal hemianopia attributable to optic chiasm damage.[65]

Visual field defects can also result from blast injury and in a sample of 61 such patients, 15% exhibited a hemianopia or quadrantanopia while 36% exhibited a global visual field loss.[66] Poor VA and pupillary dysfunction were also associated with the field defects. Moreover, field defects have been compared in military personnel after non-blast and blast-induced injuries[67], multiple scattered defects being present in 48% of individuals in both groups and field defects becoming more severe over time. Field defects can also be caused by low-level blast exposure during military training. In a study of nine instructors who were exposed to the blast versus four 'breacher' engineers who were not, the instructors exhibited higher vertical deviations at near compared with controls and decreased visual field sensitivity in the left eye.[68]

Pupillary function

Pupillary response in the acute stage of a TBI can been used to indicate treatment options[69], infra-red pupillometry (IRP) providing a scaler value to pupillary function, viz. the neurological pupil index (NPi), return to normal values suggesting general pupillary function should improve. It has also been suggested that the NPi score should be included in the clinical examination of TBI patients as a sensitive, non-invasive means of monitoring pupillary function in both acute and chronic cases.[69] In a study of TBI patients in Portland, Oregon in the period 2012 – 2013, five patients were identified with pupillary problems, two of which had consistently abnormal NPi

scores and underwent intracranial pressure monitoring while two patients showed early improvement in NPi and were associated with more normal pupil reactivity.[69] In addition, in a study of 17 non-blast associated TBI cases and 15 controls, pupil responses were obtained to a step-wise change in light stimulus.[70] The TBI patients showed a deficit on a number of measures including maximum and average constriction velocity, average delay, and maximum diameter and amplitude of constriction suggesting adverse effects of TBI on the autonomic nervous system.

Accommodation

Accommodation problems interfere with the ability to focus the eyes clearly on objects at different distances. Dysfunction of the accommodative system has been reported in mild TBI with accommodative insufficiency, i.e., a decrease in amplitude of accommodation, being the major defect.[71,72] Similarly, in pre-presbyopic TBI patients, accommodative dysfunction and insufficiency were observed in 24.4% and 41.1% of patients respectively.[73,74] In addition, a study comparing 50 blast related TBI and 50 non-blast related TBI patients found similar degrees of accommodative problems among subjects.[28]

Eye movement

Eye movements are involved in multiple visual functions including maintaining fixation, tracking moving objects, and when reading or driving. Eye movement dysfunction is reported in about 90% of patients suffering a concussion or blast injury, conjugate eye movements appearing to be the most affected.[75] Hence, functional magnetic resonance imaging (fMRI) studies of oculomotor control nuclei during vergence and saccadic eye movement have revealed bilateral signals in control patients originating in the superior colliculus and oculomotor and abducens nuclei, such signals being significantly reduced in chronic TBI.[76] Various pathological changes have also been observed in the midbrain in some cases of CTE affecting the superior colliculus and associated nuclei and in fiber tracts controlling eye movement[77] (Fig 1). In addition, examination of eye movement enables higher cortical functioning and the involvement of many diffuse brain pathways to be assessed.[72] A sensitive eye movement test, often used on the sidelines of sporting

venues, is the King-Devick test which can rapidly reveal slowed reaction times in cases of acute concussion.[72,78] Early-eye movement dysfunction may also distinguish between patients suffering post-concussion syndrome (PCS) from non PCS.[79]

A number of studies have suggested that patients with TBI have problems with vergence eye movements, i.e., binocular eye movements which track moving objects in depth, a process which involves complex neurological processing.[73] The prevalence of convergence insufficiency (CI), in which the eyes may drift outwards during close work resulting in eye strain, blurred vision, and diplopia, was tested retrospectively in a large sample of 557 civilian patients with TBI with or without other recorded visual symptoms.[74] Approximately 9% of patients exhibited CI without a saccadic or pursuit eye movement problem, eye muscle nerve palsy, visual field defect, vestibular dysfunction, or nystagmus. CI is also a common binocular vision defect after concussion attributable to sports injury, and in a sample of 78 athletes evaluated one month after injury, was present in 42% of the sample.[80] The presence of CI has also been linked to slower reading speeds, compromised attention, and impaired performance at work.[80] TBI associated with a loss of consciousness can also have focal effects on the brain stem and therefore affect eye movement. In a study of 123 normally sighted individuals, 28 with diffuse TBI, abnormal vergence movements were observed in the TBI patients attributed to damage to the oculomotor control system.[76]

A variety of techniques have been used to study saccades in TBI. A head mounted video-based eye tracker has been used to study military veterans with PCS.[81] In those with mild TBI, larger position errors, reduced saccadic amplitudes, smaller predicted peak velocities, longer durations, and less ability to follow a moving target were observed. A portable saccadometer has also been used to measure saccades with significantly increased reaction times being observed one-week post-injury and with no significant change after a follow-up period.[82] The most common focal lesion associated with TBI is located in the frontal lobe and measurement of anti-saccades, in which eye movements are deliberately made in a direction opposite to the visual stimulus, and remembered saccades in which the eyes move towards a remembered point without a visual stimulus, may be an effective neuro-ophthalmological method of testing frontal lobe function. Infra-red oculography (IRO) was used to study

saccades in 25 patients with TBI.[83] Although visual reflexes were inhibited, initiation of voluntary saccades, in which gaze was deliberately directed towards a stimulus, was not disturbed. Nevertheless, concussed athletes exhibit longer latencies in saccadic tasks, increased position errors, and fewer numbers of self-paced saccades compared with controls.[84] In addition, functional magnetic resonance imaging (fMRI) of these patients revealed recruitment of additional brain regions and larger areas of activation compared with controls. In follow-up studies, concussed patients who exhibited defects in anti-saccades, self-paced saccades, and memory-guided saccades improved their performance after the acute phase compared with controls although there were persistent deficits even after 30 days.[85] Eye movement problems may also depend on the severity of injury. In 37 TBI patients (20 mild, 17 moderate to severe) and 19 controls, increasing latency and reduced accuracy of visually-guided saccades were more pronounced in the moderate to severely affected group while more pro-saccade errors were present in both groups.[86] As a consequence, anti-saccadic performance may help in the assessment of injury in TBI, significant deficits in anti-saccadic latency and pro-saccadic error duration being correlated with loss of white matter integrity in the splenium of the corpus callosum.[87] In addition, predictive saccades, in which the eyes track a moving target, were used to assess the integrity of the frontal-striatal pathways[88] while Williams et al.[89] showed that the rate of self-paced saccades was correlated with visually guided neuropsychological tests.

Smooth pursuit movements can also be affected in TBI. Murata et al.[90] studied dynamic visuo-motor synchronization between patient gaze and its target during visual tracking using EYE-TRAC, a device which quantifies the time taken to predict the location of the target. In mild TBI, scores were worse than in 95% of controls while in acute TBI, initially abnormal scores were followed by an improvement. In further studies of target location prediction during pursuits, TBI patients exhibited poorer prediction and position errors were increased, performance being correlated with the 'California verbal learning task (CVLT-II)', a widely used test of episodic verbal learning and memory, suggesting pursuit eye movement as a sensitive method of testing cognitive functioning.[91] Visual tracking may also be directly related to pathological changes associated with TBI. Hence, gaze error during a circular visual tracking task was related to mean functional anisotropy, i.e. the non-homogenous physical properties of white matter obtained by DTI.[92] Eye tracking performance in

mild TBI can also be affected by the degree of additional cognitive 'load' they experience during the task.[93]

Critical flicker fusion frequency threshold (CFFF)

The critical flicker fusion frequency (CFFF) threshold is the frequency at which a flickering light stimulus appears as a steady light. Schrupp et al.[94] studied CFFF at the fovea and at a horizontal eccentricity of 10° in 14 mild TBI and 29 controls, TBI patients exhibiting reduced sensitivity and an increasingly variable response which was attributed to damage of higher cortical pathways.

Vestibulo-ocular reflex (VOR)

The vestibulo-ocular reflex (VOR) is a reflex eye movement that stabilizes images on the retina during movements of the head. This is achieved by the central nervous system which induces an eye movement in the opposite direction to that of the head. It can be tested by the 'rapid head impulse test' in which the head is rapidly moved to the side. Normally the eyes will remain looking in the same direction but in some disorders such as progressive supranuclear palsy (PSP), no compensatory eye movement may be apparent.[95] A useful indicator of VOR function is the dynamic visual acuity (DVA) test which can measure the degree of gaze stability in a variety of clinical settings.[96,97]

A number of studies suggest that the VOR may be affected by TBI. In symptomatic military personnel, a variable response to VOR gain has been reported during high velocity head movements suggesting damage to vestibular pathways.[98] In addition, in children and adolescents with sport-related concussions and PCS, VOR dysfunction was present in about 28% of patients. As severe TBI can also affect the brain stem and potentially VOR, eye movements using video-oculography (VOG) during galvanic labyrinth stimulation are often made within three days of an injury to predict prognosis.[99] Furthermore, in patients with more severe brain damage, labyrinth stimulation revealed that the VOR was present in approximately 50% of patients tested but absent in the others.[100]

Nystagmus

Nystagmus has been reported in TBI most commonly as a result of vehicle accident.[102] Such incidents can result in injuries originating from several directions including rear-end, frontal, and lateral impacts. Hence, in a sample of 65 patients with whiplash injuries, those with trauma affecting the cervical spine and originating from frontal or rear-end collisions, suffered pathological central nystagmus disinhibition while those suffering cross-collision impacts exhibited both vestibular and sensory disturbance.[101] In addition, in a blast-exposed group of military personnel experiencing dizziness, abnormal nystagmus was observed in about 50% of patients whereas in non-symptomatic patients, the frequency of nystagmus was 33%.[98]

Electrophysiology

Evoked potentials (EP), especially visual evoked potentials (VEP) and somatosensory evoked potentials (SSEP), have been consistently used to monitor survival and functional recovery in severe TBI.[102] The pattern VEP stimulus is especially useful in the objective assessment of visual system defects and in recovery.[103] In addition, the electroretinogram (ERG) has been used to assess the effectiveness of the GCS as an indicator of prognosis of patients at discharge from hospital.[104]

Changes in the ERG have been reported in a variety of disorders and therefore, potentially useful in assessing the function of retinal ganglion cells after TBI.[20] Freed and Hellerstein[103], however, reported in mild TBI that full-field ERG was not affected. However, neutral-position pattern ERG (PERG) was studied after blast exposure and resulted in a bimodal response, temporal recovery four weeks post-injury leading to persistent dysfunction 12 weeks later.[105] In addition, a modification of the PERG was used to test the effect of changes in posture, responses being correlated with the light-evoked activity of retinal ganglion cells.[105]

An early study identified a ‘post-trauma vision syndrome’ (PTVS) in TBI characterized by binocular vision dysfunction, diplopia, blurred vision, vertigo, and a ‘hallucination-like’ experience.[106] The pattern VEP P100 was studied in 10 such patients and 10 controls, the amplitude response being affected by dysfunction of the

sensory-motor feedback loop. Additional treatments such as base-in prism and bi-nasal occlusion improved responses in these patients.[106] The VEP can also be affected by more complex stimuli, e.g., changes in texture, orientation, or motion of the stimulus and can identify cortical damage not revealed by standard clinical methods.[107] Hence, Yadov and Cuiffreda[108] investigated the effect of check size and contrast on the pattern VEP in mild TBI suggesting differential effects on visually symptomatic and asymptomatic patients. It was concluded that a 20 mm of arc check size was optimal for VEP testing in TBI. The effect of treatments such as binasal occlusion and base-in prisms on the VEP in each eye was also studied by Yadav and Cuiffreda[109], only binasal occlusion resulting in an improvement in VEP amplitude. Visual attention can also be quantified using the VEP. Hence, differential attenuation of the alpha-band was measured in mild TBI, with and without self-reported deficits, abnormal attenuation being observed in those individuals with attentional deficits.[110]

Studies have suggested that event-related potentials (ERP) may also be useful in the study of TBI.[111] Lower-level complex information processing was studied in mild TBI using the ERP and a typical 'oddball' paradigm in which a rare stimulus is interspersed among a common stimulus. Patients exhibited increased latency and reduced amplitude of those components involved in the recognition of texture and cognition, suggesting selective deficits in complex visual processing as a result of TBI, which could impair work performance.[112] In addition, a study of 11 TBI patients and 11 controls using a primary colour discrimination task demonstrated an increase in latency and reduced amplitude of the P300 response but no differences in response accuracy or reaction time.[58] Attention deficits have been investigated in 11 TBI patients with closed head injury one year after trauma and 14 controls.[113] Subjects carried out a continuous vision reaction time discriminating task while ignoring task-irrelevant stimuli, TBI patients showing attenuation of mismatch negativity, a delayed P1 component, and reduced amplitude of the N165 and P3B components involved in attentive information processing. ERP in combination with fMRI has also been used to distinguish whether the symptoms attributable to mild TBI were a result of cerebral dysfunction or psychological disturbance. Hence, in a study of 14 patients and 23 controls, patients exhibited greater ERP deficits associated with greater blood oxygen attenuation levels suggestive of cerebral dysfunction.[114]

Sleep problems

Sleep disturbance is common after TBI.[115] In a sample of 87 TBI cases ranging from mild to severe, sleep disturbance was found to be greatest in the mildly-affected group.[116] Sleep problems frequently affected non-rapid eye movement sleep (nREM) and were accompanied by changes in EEG spectral power, the presence of slow waves, and effects on sleep spindles.[117] The authors also concluded that enhanced nREM accompanied by increased 'β' waves may indicate brain injury or the presence of pain and anxiety.

Visual perception

Visual perception in TBI has been studied using a variety of different tasks.[117] Patients with TBI were impaired on many of these tasks and exhibited deficits in response time and accuracy suggesting various aspects of visual perception are affected in TBI, with the possible exception of object recognition. In addition, in a task which involved locating items in different types of display, there were no significant differences between TBI and controls.[118] Reaction time measures are particularly sensitive to the increasing complexity of the stimuli. Perception of sine-wave gratings defined by first and second-order characteristics was studied in 15 patients with mild TBI and 15 controls, reaction times being longer in mild TBI accompanied by an increased variability of response.[119]

Motion vision (Akinopsia)

Loss of motion vision ('akinopsia') has been observed in TBI patients with otherwise normal visual function. Pelak and Hoyt[120] studied two patients with a conscious loss of visual motion attributed to brain lesions affecting extrastriate visual cortex. Patients with mild TBI often complain of increasing sensitivity to visual motion. Hence, the 'coherent motion threshold' (CMT) was measured using dynamic random dots in 14 mild TBI patients and 40 controls, a progressive increase being observed in TBI with increasing development of complex symptoms dependent on motion sensitivity and degree of vertigo.[121] It was concluded that there were changes in the

magnocellular visual pathway involving visual area V5 and areas in the medial temporal lobe involved in motor processing.

Visuo-spatial function

In a study of 13 TBI patients and 10 controls, patients with TBI exhibited poorer performance on visuo-spatial tasks such as maze learning.[122] In addition, in a study of 30 mild TBI patients and 30 controls, verbal and visuo-spatial working memory were impaired[123] and in a study of visual object space perception, poorer performance was correlated with the degree of self-reported difficulties.[124]

Reading ability

In 214 TBI patients in which reading ability was tested 1, 6, and 12 month post-injury, performance of younger patients was impaired at 1 and 6 months while older patients were also impaired at 12 months.[125] A variety of reading problems have been recorded including loss of place, skipping of lines, and difficulties in moving to the next line.[126] In 24 college students with ABI (12 with traumatic and 12 with non-traumatic injury), both groups cited problems with reading comprehension and academic performance post-injury.[127] Hence, mean performance of reading tests was low to average and the deficits correlated with the CVLT.

Complex syndromes

In rare cases, patients with TBI may develop the visual symptoms characteristic of a more complex visual syndrome such as 'Balint's syndrome'. These include a psychic paralysis of gaze (‘ocular apraxia’), lack of muscular coordination (‘optic ataxia’), e.g., an inability to guide the hand towards an object using visual cues, and a spatial disorder of attention ('simultanagnosia'), viz. an inability to report all items or their relationships in pictures depicting events or situations.[128,129] In addition, cases of ‘prosopagnosia’ have been reported in TBI associated with focal lesions in the left-posterior hemisphere.[54,130] A TBI patient with a corrected VA of 20/70 and normal colour vision had poor shape determination skills and a poor ability to match unfamiliar faces, although matching of facial expression was preserved. Another TBI

patient could describe or demonstrate the use of objects but could not name them or sort them into categories.[131] The impairment appeared to be specific to vision naming and developed later into a problem of naming letters, ultimately resulting in optic aphasia and alexia. Facial expression is important in communication, especially in conveying information and emotion. Hence, in 12 patients with severe TBI, there were considerable difficulties in interpreting facial expression and consequently in communication.[132] In another case, an individual exhibited severe perceptual difficulties in recognizing non-facial stimuli but recognition of faces, especially those of celebrities, was well preserved.[133]

Visual hallucinations

Visual hallucinations have been reported in several neurodegenerative disorders, especially in individuals with impaired VA or with a more severe cognitive impairment[20] but have been less studied in TBI. However, symptomatic acoustic-based hallucinosis has been observed in TBI after damage to various subcortical regions.[134] In addition, neuropsychological and cognitive disturbances are common after TBI[135] and it is possible that visual hallucinations may be present especially in those with more severe damage and poor VA.

Discussion and conclusions

Various aspects of vision are likely to be affected as a consequence of TBI with many patients exhibiting multiple visual defects (Table 2).[27] These include aspects of primary vision such as VA[52,53], which although not affected in all patients, can be a persistent deficit in some.[54] Visual field loss is characteristic of TBI and includes hemianopia and quadrantanopia accompanied by poor VA and pupillary dysfunction.[10,28,55,62,63] There is little evidence that colour vision is affected although this remains a poorly investigated aspect of TBI.[58] Defects in stereopsis may be present in a significant number of patients which may be caused by cortical damage rather than a binocular vision problem.[59] Eye movement problems are a frequent feature of TBI and may be an early visual symptom with various measures of saccades[83-87], pursuits[91,92], and vergence eye movements including CI being reported.[67,68,70,74] Nystagmus has been reported especially after vehicle accidents and

in military personnel exposed to blast injury.[98,101] Impaired VOR may be seen in a variety of circumstances but most frequently in military personnel and in sport-related concussion.[98] Electrophysiology may be useful in investigating and evaluating TBI and a variety of effects on the VEP[106,108-110] and ERP[111-113] have been reported, although there is less available information regarding the ERG.[103] Complex visual functions are commonly affected including various aspects of visual perception[117-119], motion vision[120,121], and visual-spatial function[122,123] but whether visual hallucinations consistently occur in TBI remains to be investigated.[134-135] Monitoring of visual functions will be necessary in TBI patients as some visual functions may improve and others worsen over time.

Neurologic, neuropsychological, and social interaction problems can significantly impair the ability of a patient with TBI to sustain subsequent employment.[130] In a study of 520 military veterans assessed 15 years after a penetrating head injury as a result of combat in Vietnam, 56% were in employment compared with 82% of the uninjured population.[136] Visual field loss and verbal memory problems appeared to be the most significant variables correlated with ability to work. Given the complexity of possible defects, many of the available assessment scales may not be adequate to assess all facets of regional support that may be required.[137] However, the eight-category care-needs scale (CANS) may be a sensitive and valid measure to assess care and support needs.[137] In addition, Radomski et al.[138] have described a vision screening program for military personnel which considered for inclusion 29 visual tests. Nine such tests were subsequently selected for screening including functional performance, self-reported problems, far/near VA, visual fields, reading, accommodation, convergence, binocular vision, saccades, and pursuit movements. In addition, health and vision QOL questionnaires are important as an addition to clinical measures such as perimetry, the 'Health and vision-related QOL' assessed by NEI-VFQ in particular being a valuable measure of self-reported visual impairments in patients with visual field defects.[139]

Patients with mild TBI may suffer a variety of visual problems in combination with a decline in ocular and overall health.[140] As a result, patients may benefit from vision rehabilitation including the prescribing of spectacles with a variety of tints, and prism combinations (Table 3). In addition, chronic photophobia in TBI may be treated using

light-filtering lenses.[57] Contrast sensitivity and reading rate also increased with the addition of photochromic lenses compared with near point optical correction alone.[57] Patients with chronic visual dysfunction after TBI may require additional occupational, vestibular, cognitive and other forms of physical therapy.[140] The use of eye movement recording techniques using computer based stimuli has been particularly useful in studying reading problems of patients with TBI. Hence, reading-related oculomotor rehabilitation was studied in nine patients with TBI using single-line and multi-line simulated reading, and recording fixation, saccades and pursuits.[141] All patients reported improved performance after rehabilitation which was confirmed by measures of oculomotor function. In a more recent study, oculomotor function and reading were studied in 12 mild TBI patients undergoing oculomotor training[142], training of different types of eye movement being given in a random order. It was concluded that oculomotor rehabilitation training had a strong positive effect on oculomotor control and on overall reading ability. Deficits in gaze control may also influence 'stepping behavior' and increase the risk of trips or falls while climbing stairs[143], balance and eye movement training and visual awareness exercises may help to control these problems. The use of driving simulators designed for stroke victims may also help to overcome problems in the evaluation and rehabilitation of driving following TBI.[144]

Future research should concentrate on three main areas. First, sensitive and reliable tests are needed to detect the often subtle changes that may be associated with concussion and sub-concussive repetitive injury.[73] In this regard, tests involving the visual system, especially of eye movements, which can assess higher brain function and various diffuse brain pathways, may be especially useful. Second, some visual functions have been poorly studied in TBI, e.g., colour vision, some aspects of electrophysiology including the ERG, and whether visual hallucinations are a characteristic feature of TBI. Third, further research on the possible relationship between TBI and a variety of neurodegenerative diseases such as AD, CTE, and Parkinson's disease including a comparison of the visual problems reported in these disorders with those arising from TBI may be particularly informative.

In conclusion, TBI is associated with a variety of visual problems, including defects in VA, visual fields, eye movement, and in more complex aspects of vision involving

visual perception being most typical. Patients may experience multiple visual problems in combination with a decline in ocular and overall health. Such patients may benefit from vision rehabilitation including the prescribing of spectacles with a variety of tints and prism combinations. In addition, patients with chronic visual dysfunction after TBI may require occupational, vestibular, cognitive, and other forms of physical therapy.

Conflict of interest statement

The author reports no conflicts of interest and has no proprietary interest in any of the material mentioned in this article.

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Table 1. Descriptive terms used to define traumatic brain injury (TBI)

Term	Abbreviation	Definition
Acquired brain injury	ABI	Any type of brain injury resulting from a penetrating or non-penetrating cause
California verbal learning task	CVLT	A measure or episodic learning and memory
Chronic traumatic encephalopathy	CTE	Neurodegenerative disorder which may result from repetitive brain injury
Glasgow coma scale	GCS	A 15-point scale classifying the severity of brain damage
Health and vision-related QOL score	NEI-VFQ	A means of self-reporting visual impairments
Post concussion syndrome	PCS	Persistent symptoms following TBI such as headache and irritability
Post traumatic amnesia	PTA	State of confusion following TBI
Post traumatic stress disorder	PTSD	Complex psychiatric disorder following a traumatic incident
Post traumatic visual syndrome	PTVS	Syndrome involving binocular vision dysfunction, diplopia, blurred vision, vertigo, and hallucinations
Traumatic brain injury	TBI	Injury resulting from an external force

Table 2. Summary of visual signs and symptoms reported in traumatic brain injury (TBI)

Ocular function	Change in TBI
VA	VA loss in some patients and can be persistent.[52-54]
Photophobia	May be intense, intermittent, or chronic.[29,57]
Colour vision	Few studies, but electrophysiology suggests colour vision deficits could be present.[58]
Stereopsis	Defects in a significant number of patients caused by cortical pathology rather than a binocular vergence problem.[27,59]
Visual fields	A characteristic symptom of TBI including hemianopia and quadrantanopia.[10,28,55,62,63] May be accompanied by poor VA and pupillary problems.[66]
Accommodation	Insufficiency especially in mild TBI.[28,71-73]
Pupillary function	Deficits on a number of tests of pupillary function. A sensitive test in acute TBI to decide treatment options.[69,70]
Vergence	CI is a common BV defect in TBI especially after sports concussion.[73,74,76,80]
SEM	Characteristic of TBI with deficits on various tasks including anti-saccades, self-paced saccades, and in memory-guided saccades.[81-88]
SPEM	Affected in TBI and a sensitive method of testing cognitive function.[90-93]

CFFF	Reduced sensitivity and increased variability.[94]
VOR	Affected especially in symptomatic military service members and in children/adolescents with sport-related concussion.[98]
Nystagmus	After car injury and in blast exposed veterans.[98,101]
ERG	Little evidence for significant effects.[103,105]
VEP	Affected using a variety of stimuli.[106-110]
Event-related potentials	Affected using a variety of stimuli and paradigms.[111-115]
Sleep disorders	Common after TBI usually affecting nREM.[115,116]
Visual perception	Affected with possible exception of object recognition.[117-119]
Motion perception	Loss of visual motion in some patients.[120,121]
Visuo-spatial function	Impaired in TBI.[122-124]
Reading ability	Variety of reading problems present.[125-127]
Complex syndromes	Balint's syndrome and prosopagnosia recorded in TBI.[54,128-133]
Visual hallucinations	Few studies but likely to be present.[20,134,135]

Abbreviations: CI = Convergence insufficiency, EEG = Electroencephalogram, nREM = Non rapid eye movement sleep disorder, SEM = Saccadic eye movements,

SPEM = Smooth pursuit eye movements, PSP = Progressive supranuclear palsy, VEP = Visual evoked responses, VOR = Vestibulo-ocular reflex

Table 3. Possible therapeutic interventions to treat visual problems in traumatic brain injury (TBI)

Visual feature	Therapy
Visual acuity (VA)	Prescription of spectacles with various tints and prism combinations[57]
Contrast sensitivity (CS)	May be improved by addition of photochromic lenses[57]
Photophobia	May be improved by light-filtering lenses[57]
Eye movement affecting reading	Reading-related oculomotor rehabilitation[141,142]
Gaze control	Balance training, eye movement and visual awareness exercises[143]
Driving	Use of driving simulators for evaluation and rehabilitation[144]

Legends to figures

Fig 1. Section of midbrain of a case of chronic traumatic encephalopathy (CTE) showing tau-immunoreactive pathology (brown immunolabelling) in various nuclei and fibre tracts (CA = Cerebral aqueduct, Csp = Cortico-spinal tract, FPon = Fronto-pontine fibres, ML = Medial lemniscus, MLF = Medial longitudinal fasciculus, PAG = Periqueductal gray, SC = Superior colliculus, SCP = Superior cerebellar peduncle, SN = Substantia nigra, TrN = Trochlear nucleus). Pathology is particularly evident in the SC, SN, and TrN. Tau immunohistochemistry (AT8, haematoxylin).