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Neuro-Ophthalmic Deficits after Head Trauma

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Abstract Head trauma can injure the afferent and/or efferent visual systems, resulting in neuro-ophthalmic deficits. When assessing afferent pathway injuries, a stepwise approach to evaluating visual acuity, pupils, color perception, and visual fields is critical. Traumatic optic neuropathy is of especial importance and its management must be tailored on a case-by-case basis. Efferent pathway injuries should be assessed with attention to abnormalities of ocular alignment and motility, which may occur as isolated deficits or as part of a recognizable syndrome. Concussion or diffuse axonal injuries may also affect ophthalmologic function. Here, we review the extant literature describing the assessment and acute treatment of traumatic neuro-ophthalmic deficits.

Keywords Head trauma · Optic neuropathy · Cranial nerve palsy · Visual pathway

Introduction

Head trauma commonly results in neuro-ophthalmic deficits due to injury to the afferent and/or efferent visual systems. The assessment of such patients can be quite challenging, and detailed examination may not be possible in the acute setting. Visual symptoms can be vague in patients with head trauma, and potentially masked by other neurologic deficits, which makes diagnosis more challenging. This may account for the large variations in reported frequency of neuro-ophthalmic deficits after head injury, which range from 1 %–3 % in 1 survey [1] up to 56 % in another study [2]. Clinicians can increase their ability to diagnose these deficits by taking a structured approach toward assessing the afferent and efferent visual pathways.

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Afferent Visual Pathway

The afferent visual pathway begins at the photoreceptor cells in the outer retina and ends at the primary visual cortex of the occipital lobe, with collateral input from visual association areas. All of these regions are susceptible to traumatic injury, with the resulting deficit dependent upon the location of the insult as well as the severity.

Traumatic Optic Neuropathy

The optic nerve is vulnerable to compression, traction, crush, laceration, and avulsion injuries, any of which can give rise to traumatic optic neuropathy (TON). TON can occur through a direct or indirect mechanism. Direct mechanisms anatomically disrupt optic nerve fibers, and include processes such as penetrating orbital trauma, nerve avulsion from globe, optic nerve crush injuries (typically occurring at the orbital apex), or laceration by bone fragments. More commonly, TON results from an indirect injury in which the forces (often acceleration/deceleration) produced by an orbital impact are transmitted to the nerve, leading to traction, elevated intraorbital pressure, compression by orbital hemorrhage, or optic nerve sheath hematoma, or axonal shearing [3].

Most cases of TON are believed to arise from damage to the intracanalicular segment, even in the absence of sphenoid fracture [3]. Theoretically, this may occur by a shearing injury analogous to diffuse axonal injury (DAI), possibly followed by ischemic injury as reactive edema generates compression at the orbital apex [4•], and further inflammatory injury as the

tissues respond to traumatic insult. Mouse models have shown that DAI triggers an inflammatory response with upregulation of IL-1, IL-6, and TNF- TNF-α [5], as well as T-cell infiltration and astrocyte activation [6]. This suggests that treatment of neuroinflammation may prove to be helpful in the acute and subacute management of TON.

Traumatic optic neuropathy is uncommon but not rare. In 1 review of 326 patients seen in a tertiary care Neuro-Ophthalmology service after head injury, deficits consistent with TON were seen in 12 %, with 7 % diagnosed as indirect TON [2]. In the pediatric population, a recent prospective series estimated the annual incidence of TON at ~1 case per million, with most events related to sports injuries (23 %), falls (19 %), or motor vehicle collisions (16 %) [7].

Clinical exam and appropriate neuro-ophthalmic imaging play a vital role in identifying the location and nature of the injury. Orbital computerized tomography (CT) can assess for retrobulbar hemorrhage, optic nerve sheath hematoma, and bone fragments compressing or lacerating the optic nerve. Magnetic resonance imaging (MRI) is of less utility in TON, often not showing any signal changes. However, diffusion tensor imaging (DTI), an MRI technique which tracks motion of water molecules along nerve fiber tracts, demonstrates lower axial and mean diffusivity in optic nerves with TON, acting as a biomarker of injury and potentially predicting the potential for visual recovery [8••]. In the event of a suspected metallic foreign body in the eye or in the orbit, MRI is contraindicated. Visual evoked potential testing can also be prognostic, with higher amplitude and shorter latency correlating to better final visual acuity [9].

Treatment of Traumatic Optic Neuropathy

No single treatment protocol has proven effective for TON, although several strategies exist. In broad terms, there are 4 approaches to management: observation, systemic corticosteroids, surgical decompression of the optic canal, or a combination of corticosteroids and surgical decompression. Several of the existing strategies draw inferences from treatment trials involving other forms of CNS injury (Table 1).

Steroid treatment for brain edema was introduced in the early 1960s, and became a common treatment for patients with severe TBI by the 1970s, after a randomized trial showed improved mortality rates [10]. However, several subsequent trials have failed to show appreciable benefit [11].

A series of 3 National Acute Spinal Cord Injury Studies (NASCIS I, II, and III) published from 1984–1997 showed improved neurologic recovery with high-dose intravenous methylprednisolone after spinal cord injury (excluding patients with penetrating injury, pediatric patients, and those presenting >8 h after injury) [12–15]. The NASCIS results have been challenged, citing small effect size along with increased risk of infection and gastrointestinal bleeding

Trials have been conducted to assess whether these findings are applicable to traumatic brain injury (TBI) patients. A 1997 systematic review of 13 randomized trials encompassing 2073 TBI patients found a pooled absolute risk reduction of 1.8 % with corticosteroid treatment, but noted concerns over infection and gastrointestinal bleeding [16]. The Corticosteroid Randomization After Significant Head Injury (CRASH) trial of 10,008 patients from 239 hospitals in 49 countries showed a deleterious effect of methylprednisolone therapy, with increased 2-week mortality (21 % vs 18 %) and increased relative risk of death by 6 months (1.15) in the steroid group [17–19]. Furthermore, there was no significant difference in death or disability between the steroid and non-steroid groups in the CRASH trial when stratified by injury severity, leading to the authors to conclude that corticosteroid treatment provides no benefit after head injury [19]. A statement from the Brain Trauma Foundation Task Force in 2007 asserts that "the use of steroids is not recommended for improving outcome or reducing intracranial pressure. In patients with moderate or severe TBI, high-dose methylprednisolone is associated with increased mortality and is contraindicated" [11].

There is no high quality evidence guiding management of TON. Two Cochrane reviews searching for randomized controlled trials comparing steroids, surgery, or observation alone found only 1 paper meeting inclusion criteria [20, 21]. Steroids have been used to treat TON, based on extrapolation from the NASCIS data [3, 22]. Alternatively, observation without steroids has been advocated given the results of the CRASH study [3, 22]. Surgical optic canal decompression (by orbitotomy or endoscopic approach) is also performed at some centers, citing the potential to relieve pressure in the optic canal and remove bony fragments that threaten the nerve [23]. Yang et al. reported visual acuity improvement in 40.6 % of TON patients treated with endoscopic decompression surgery after a trial of megadose steroids had failed to produce any effect [4•]. A recent retrospective series of 42 patients with TON suggested that the addition of steroid therapy after optic nerve decompression surgery did not appear to improve visual outcome [24].

The International Optic Nerve Trauma Study (IONTS) was a non-randomized, non-blinded study comparing the outcomes of methylprednisolone therapy (megadose ≥5400 mg, very high dose 2000–5399 mg, high dose 500–1999 mg, moderate dose 100–499 mg, or low dose <100 mg), surgical decompression of the optic canal (by external ethmoidectomy, medial orbitotomy, endonasal, or craniotomy), or observation alone in a comparative nonrandomized interventional study of patients with indirect optic nerve injuries [22]. The IONTS found no significant difference in visual outcome between the steroid vs surgical decompression vs observation groups, and no indication that steroid dosage or timing influenced outcome [22]. This study suffered from multiple limitations and lacks broad applicability to the general population. For

Table 1 Major trials of steroid treatment after central nervous system trauma

Author, year	Population	Interventions	Outcome
Bracken, 1984 (NASCIS I) [12]	*N*=330 Acute spinal cord injury	Randomized-controlled trial 1. Methylprednisolone 1 g/d for 10 d after injury 2. Methylprednisolone 100 mg/d for 10 d after injury	No significant difference. Slightly higher early case mortality and infection rates in high-dose group.
Bracken, 1990 (NASCIS II) [13]	*N*=487 Acute spinal cord injury	Randomized double-blind trial 1. High-dose methylprednisolone for 24 h (*n*=162) 2. Naloxone for 24 h (*n*=154) 3. Placebo (*n*=171)	Methylprednisolone group showed statistically significant improvement in motor, pinprick, and touch compared with naloxone or placebo, if treatment began within 8 h of injury.
Bracken, 1997 (NASCIS III) [14]	*N*=499 Acute spinal cord injury, within 8 h of injury	Randomized double-blind trial 1. High-dose methylprednisolone for 24 h (*n*=166) 2. High-dose methylprednisolone for 48 h (*n*=167) 3. Tirilazad for 48 h (*n*=166)	48 hr methylprednisolone showed significantly better recovery of function at 6 wk and 6 mo, but also had higher rates of sepsis and pneumonia. 24 hr methylprednisolone was equivalent to 48 hr tirilazad.
Bracken, 1998 (NASCIS III) [15]	*N*=499 Acute spinal cord injury, within 8 h of injury	Randomized double-blind trial 1. High-dose methylprednisolone for 24 h (*n*=166) 2. High-dose methylprednisolone for 48 h (*n*=167) 3. Tirilazad for 48 h (*n*=166)	At 1 yr after injury, all 3 groups showed equivalent neurologic recovery if treatment was initiated<3 hours after injury. If initiated 3–8 h after injury, the 48 h methylprednisolone arm was superior.
Levin, 1999 (IONTS) [22]	*N*=127 Traumatic optic neuropathy, within 7 d of injury	Nonrandomized interventional study 1. Various steroid regimens (*n*=85) 2. Optic canal decompression (*n*=33) 3. No treatment (*n*=9)	No significant difference between steroid therapy, surgery, and observation alone.
Roberts, 2004 (CRASH) [17]	*N*=10,008 Adults with head injury, Glasgow ≤14, within 8 h of injury	Randomized-controlled trial 1. Methylprednisolone, 2 g loading dose followed by 400 mg/h for 48 h 2. Placebo	Significantly higher all-cause mortality at 2 wk in the corticosteroid group. No significant effect related to injury severity or time since injury.
Edwards, 2005 (CRASH) [19]	*N*=10,008 Adults with head injury, Glasgow ≤14, within 8 h of injury	Randomized-controlled trial 1. Methylprednisolone, 2 g loading dose followed by 400 mg/h for 48 h 2. Placebo	Significantly higher death rate and severe disability rate at 6 months in the corticosteroid group. No significant effect related to injury severity or time since injury.

patients presenting with acute TON, clinical decisions should be made on a case-by-case basis, keeping in mind the possibility of spontaneous recovery in some patients.

Recent experiments in murine models have demonstrated that oxidative stress and inflammatory mediators play a role in TON. In 1 study, mice treated with resveratrol after optic nerve crush injury showed lower levels of superoxide and improved retinal ganglion cell (RGC) survival [25]. Other investigators have shown that in certain cytokine environments (eg, through manipulation of ciliary neurotrophic factor, leukemia inhibitory factor pathways, and crystallin upregulation), mature RGCs can be induced to actively regenerate after optic nerve injury [26–29]. It remains to be seen whether these findings can be translated into clinical applications for human subjects.

Delayed Optic Nerve Impairment

In the days to weeks after trauma, vision loss can potentially progress due to direct edematous compression within the orbit or optic canal, contusion necrosis, or papilledema caused by elevated intracranial pressure, which arises from cerebral edema and/or impaired cerebrospinal fluid absorption. Shrinkage of the optic tract can be seen by MRI, while progressive thinning of the retinal nerve fiber layer has been demonstrated with optical coherence tomography [30]. Optic nerve pallor does not develop until ~4–6 weeks after pre-genicular afferent pathway injury, so the optic nerve may appear normal for nearly 1–2 months after even a severe insult.

Optic Chiasm

The optic chiasm is anatomically privileged, so very few patients survive after sustaining trauma severe enough to injure the chiasm. A retrospective review of 19 patients with traumatic chiasmal syndrome found that the typical mechanism of injury was high-velocity impact from motor vehicle accidents or falls, causing frontal or basal skull fractures or closed head injuries with intracranial hemorrhage [31]. Within

the series, 74 % of patients had final visual acuity of 20/60 in the better eye, while 53 % of patients had no light perception in the worse eye [31]. Visual deficits due to chiasmal syndrome are typically bilateral although the findings can be asymmetric.

Optic Tract

The optic tract carries uncrossed fibers from the temporal retina of the ipsilateral eye and crossed fibers from the nasal retina of the contralateral eye, coursing from the chiasm to synapse in the lateral geniculate nucleus. Optic tract injuries are typically accompanied by other cortical deficits, but focal deficits of the tract alone have been reported [32]. Neuro-ophthalmic findings include homonymous hemianopia (classically incongruous) and contralateral relative afferent pupillary defect. In 1 study, optic tract lesions comprised 11 % of traumatic homonymous hemianopias [33].

Posterior Visual Pathways

Injury to the lateral geniculate nucleus, optic radiations, and occipital/visual cortex occurs by a variety of mechanisms including axonal shearing, focal or diffuse intracranial hemorrhage, or ischemia. In many patients, multiple overlapping visual deficits may occur, and the mechanisms of injury may be multi-factorial. A retrospective review of 160 individuals with TBI found visual field deficits in 39 %, with 22 % of individuals showing homonymous defects [34]. Clinical findings of posterior visual pathway damage include homonymous field deficits which are more congruent for lesions located further posteriorly. Higher order visual processing deficits may also be present, including alexia, agnosia, simultagnosia, or cerebral achromatopsia. Patients with higher order deficits may have a "normal" eye exam, but still present with complaints related to visual functioning. Visual rehabilitation programs have been shown to improve functioning in many cases [35•, 36–39].

Concussion and Diffuse Axonal Injury

Diffuse axonal injury (DAI) is a hallmark of TBI, often manifesting as cognitive dysfunction [40]. The diffuse nature of a concussive injury can cause impairment of attention, language, and motor control. The visual system may be preferentially affected in patients with concussion, leading to screening strategies which target eye movements and visual processing for early detection of concussive brain injury. The King-Devick test, which is administered by asking the patient to read numbers aloud from test cards while measuring the speed of rapid number naming, has been suggested as a reliable and accurate method for concussion screening in the acute setting [41•].

Recent MRI studies using the DTI technique have shown that relative anisotropy and axial diffusivity are reduced for 1–4 days after trauma (corresponding to demyelination and edema), with relative anisotropy remaining decreased 1–4 weeks later (persistent axonal injury) [42]. Relative anisotropy on DTI parallels silver stain uptake into injured tissues seen histologically [43•]. In 1 study of TBI patients, the global anisotropy value on DTI was found to correlate with the degree of impairment on clinical tests of memory function and mental processing speed [44]. The amount of signal intensity contrast between gray matter and white matter on T1-weighted MRI after TBI also correlated to the degree of memory impairment seen clinically [44]. Overall, this means that DTI has the potential to help clinicians gauge the time since injury, histologic severity of injury, and possible prognosis with regard to certain cognitive outcomes.

Among TBI patients, the extent of neurocognitive impairment tends to correspond to the degree of DAI in the frontal and temporal lobes [45]. Unfortunately, the frontal lobe is the primary site of injury in many mechanisms of TBI, including motor vehicle collisions (MVC). In 1 study evaluating the extent and distribution of DAI after MVC, the frontal lobe was the primary locus of DAI in 123 of 170 patients [46]. Such injury can impair the function of the frontal eye fields, leading to impaired visual attention and delayed voluntary saccades, although these deficits were found to improve over time in 1 functional MRI study [47].

In recent years, several studies have focused on therapeutic targets that may decrease the cortical damage caused by DAI. Erythropoietin (EPO) has demonstrated neuroprotective effects in lab models of hypoxia or trauma, as well as in vitro and in vivo models of glaucomatous optic nerve damage [48]. A double-blind, randomized controlled trial of subcutaneous EPO in 54 patients with traumatic DAI found that patients receiving recombinant human EPO demonstrated earlier improvement in their Glasgow Coma Scale scores and maintained better scores throughout a 2 week study period [49•]. Larger trials with longer follow-up are needed to understand this effect more fully, and trials specific to TON would be invaluable.

Efferent Visual Pathways

For diagnostic purposes, the efferent pathways can be subdivided into discrete structures that give rise to specific deficits when injured, and regions of the central nervous system that produce recognizable syndromes after injury (Table 2). Many of these injuries lead to ocular misalignment and symptomatic diplopia.

The ocular motility examination is particularly challenging in head injured patients since voluntary responses may not be possible. However, ocular motor deficits elicited by a careful exam can be exquisitely localizing. The examiner should

Table 2 Efferent visual pathway injuries

Deficit	Symptoms and examination findings	Diagnostic maneuvers
Skew deviation	Vertical binocular diplopia. Testing reveals comitant or incomitant vertical deviation, with or without torsional abnormalities (higher eye usually incyclotorted, unlike CNIV palsy).	ACT, MRT
Thalamic esodeviation	Horizontal binocular diplopia. Testing reveals comitant esodeviation.	ACT, MRT
Dorsal midbrain syndrome	Any combination of limited vertical gaze (usually upgaze), upper eyelid retraction in primary gaze, and mid-dilated pupils with light-near dissociation.	Versions, eyelid position measurements, and pupil testing to light vs near
CRN	Globe retraction and convergence when the patient attempts upward saccades, due to co-contraction of the extraocular muscles.	Downward-rotating optokinetic drum to elicit upward saccades
Convergence insufficiency	Horizontal binocular diplopia, which increases when the patient attempts near work. Testing reveals a relative exotropia when fixating at near.	ACT while fixating on a distant target then on a near target
INO	Ipsilateral abduction deficit, slowed adducting saccades in 1 eye and abducting nystagmus in the other eye.	Versions, with attention to saccades and nystagmus
Central vestibular nystagmus	Any of a variety of nystagmic eye movements.	Fast-beating phase may help localize: downbeat (CMJ), upbeat (medulla), PAN (nodulus), CRN (dorsal midbrain).
Nuclear CNIII palsy	Bilateral eyelid ptosis, contralateral supraduction deficit (may cause diplopia in upgaze), ipsilateral deficits of MR, IR, IO, SP.	Versions, ductions, ptosis evaluation, pupil exam
Divisional CNIII palsy	Superior: eyelid ptosis, ipsilateral SR impairment (vertical binocular diplopia). Inferior: Binocular diplopia (vertical, horizontal, and/or oblique) due to ipsilateral impairment of MR, IR, IO. Dilated pupil *without* RAPD, due to SP impairment.	Versions, ductions, pupil exam.
CNIV palsy	Torsional binocular diplopia, impaired downgaze in adduction.	Parks-Bielschowsky Three Step Test
CNVI palsy	Horizontal binocular diplopia in gaze toward the affected side, due to abduction deficit. Nuclear CNVI palsies may also have INO (MLF involvement), and impaired ipsilateral eyelid closure (CNVII fascicular involvement).	Versions, ductions, eyelid function exam, and attention for deficits suggestive of INO. Fundus exam for papilledema.
Horner's syndrome	Ipsilateral pupillary miosis (greater anisocoria in darkness than in light) due to impaired sympathetic input to DP. Ipsilateral eyelid ptosis (mild, with preserved LPS function).	Pupil exam, ptosis evaluation.
Cavernous sinus syndrome	Binocular diplopia and ipsilateral numbness in V_1 and V_2 dermatomes. Exam findings are consistent with involvement of CNIII, CNIV, CNVI, and the ophthalmic and maxillary divisions of CNV. May bilateralize if cavernous sinus pathology enlarges.	Versions, ductions, ptosis evaluation, pupil exam, and sensory testing of V_1 and V_2.
Orbital apex syndrome	Binocular diplopia and ipsilateral numbness in V_1 dermatome only. Exam findings are consistent with involvement of CNIII, CNIV, CNVI, and the ophthalmic division of CNV. Does not bilateralize.	Same testing as Cavernous sinus syndrome

ACT alternate cover test, *CMJ* cervico-medullary junction, *CNIII* third cranial nerve, *CNIV* fourth cranial nerve, *CNV* fifth cranial nerve, *CRN* convergence-retraction nystagmus, *DP* dilator pupillae muscle, *ICP* intracranial pressure, *INO* internuclear ophthalmoplegia, *IO* inferior oblique muscle, *IR* inferior rectus muscle, *LPS* levator palpebrae superioris muscle, *MLF* medial longitudinal fasciculus, *MR* medial rectus muscle, *MRT* Maddox rod test, *PAN* periodic alternating nystagmus, *SP* sphincter pupillae muscle, V_1 ophthalmic branch of CNV, V_2 maxillary branch of CNV

assess versions (conjugate movements of the eyes), ductions (individual eye movements), the horizontal and vertical vestibulo-ocular reflex (to assess brainstem integrity), and the presence or absence of nystagmus. Symptomatic binocular diplopia arising from eye misalignment can often be relieved with prismatic lenses, strategic botulinum toxin injection, or eye muscle surgery [50•, 51–53].

Cerebral Cortex

Supranuclear pathways can be damaged by TBI, including the corticobulbar pathways driving volitional eye movements and the vestibular inputs modulating eye movements with respect to head position. Several well-defined syndromes have been described, including skew deviation and thalamic esodeviation.

Brainstem

Midbrain and/or pontine injury can produce symptomatic diplopia, pupillary abnormalities, or impaired eyelid function. Such injuries can occur by high-force direct impact near the occiput or skull base, or indirectly by edematous compression, uncal herniation, or hemorrhage. Neuro-ophthalmic syndromes associated with traumatic brainstem injury include dorsal midbrain syndrome, convergence-retraction nystagmus, convergence insufficiency, and central vestibular

nystagmus. Internuclear ophthalmoplegia (INO) can also occur if the medial longitudinal fasciculus (MLF) is injured by brainstem trauma

Third Cranial Nerve (CNIII)

In 1 series, CNIII palsies accounted for 20 % of diplopia after head trauma [54]. In another, the presence of CNIII palsy was correlated to higher head trauma severity, as measured by the Glasgow Coma Scale, imaging features, and frequency of inpatient rehabilitation [55]. The diagnosis of CNIII palsy is usually straightforward, as patients have ptosis, limitation of elevation, depression, and adduction, with variable pupillary mydriasis on the affected side. The anatomy of CNIII gives rise to highly localizing forms of CNIII palsy. Midbrain injury results in nuclear CNIII palsy, characterized by bilateral eyelid ptosis, vertical diplopia due to a contralateral supraduction deficit, and ipsilateral deficits of the medial rectus, inferior rectus, inferior oblique, and sphincter pupillae. Trauma involving the cavernous sinus, orbital apex, or orbit gives rise to divisional CNIII palsy. Superior division injuries produce ipsilateral ptosis and impaired upgaze. Inferior division damage impairs ipsilateral pupil constriction, giving a dilated pupil *without a* relative afferent pupillary defect. It also impairs adduction, downgaze, and excyclotorsion of the eye, resulting in vertical and torsional binocular diplopia

Fourth Cranial Nerve (CNIV)

Of the ocular motor nerves, CNIV has the longest unprotected intracranial course and the fewest axonal fibers, making it vulnerable to injury even in mild-to-moderate head injuries [55]. In 1 series, 32 % of traumatic motility deficits stemmed from CNIV palsy [54]. Clinical features of CNIV palsy include torsional diplopia and impaired downgaze in adduction which tends to be especially symptomatic when reading.

Sixth Cranial Nerve (CNVI)

CNVI may be the most commonly affected cranial nerve in head trauma patients, sustaining damage even with low-level head injuries and accounting for 48 % of palsies in 1 series [54, 55]. Clinical deficits of CNVI palsy are esodeviation and impaired abduction of the ipsilateral eye. . Studies of traumatic CNVI palsy show spontaneous recovery rates of 12 %–38 % in bilateral cases and up to 84 % in unilateral cases [56]. Predictors of non-recovery included presence of bilateral palsy and inability to abduct past midline at the time of presentation. Management by observations, prisms, patching, or botulinum injection did not influence the final recovery rate [57, 58].

Injury to the nucleus of CNVI can impair the input to the MLF, thereby causing an ipsilateral gaze palsy. Nuclear CNVI damage is often associated with ipsilateral facial weakness due to injury of the nearby CNVII genu. The sixth nerve is vulnerable to caudal displacement of the brain due to elevated intracranial hypertension. In some patients, the sixth nerve palsy may be a “false localizing sign”, suggesting a brainstem lesion when the cause is actually intracranial hypertension. Careful fundus examination in any patient with CNVI palsy is essential to detect optic nerve swelling indicative of intracranial hypertension.

Sympathetic Pathway

Sympathetic fibers supplying the dilator pupillae muscle and eyelid Müller muscle travel from the hypothalamus to spinal cord C8-T2 (1st order), then synapse and ascend with the sympathetic chain (2nd order), synapse in the superior cervical ganglion, then travel with the carotid artery (3rd order) into the cranium, through the cavernous sinus travelling briefly with CNVI, and ultimately into the orbit to finally reach the iris dilator and the eyelid retractors. Horner syndrome can arise at any point in the pathway after trauma, and may be an indicator of a more critical underlying injury such as traumatic carotid artery dissection. Clinical findings of sympathetic pathway injury include ipsilateral pupillary miosis and eyelid ptosis.

Cavernous Sinus

The cavernous sinus is a point of convergence for multiple cranial nerves, sympathetic fibers to the head and eye, the internal carotid artery, and the dural venous system. Trauma can affect the cavernous sinus in several ways, many of which have delayed presentation. Carotid cavernous fistula is a rare vascular complication of head injury, with an overall incidence of 4 % in a series of patients with skull base fractures, and up to 8 % of middle cranial fossa fractures [59]. Trauma can also cause internal carotid artery aneurysm, cavernous sinus thrombosis, or cavernous sinus infection ascending from the paranasal sinuses after facial fractures. Neuro-ophthalmic findings of cavernous sinus pathology include a combination of sensory deficits, motility deficits and/or pupillary deficits associated with CNIII, CNIV, the ophthalmic and maxillary branches of CNV, CNVI, and sympathetic pupillary innervation. CNVI tends to be affected the earliest and most severely due to its unprotected location within the venous space of the cavernous sinus. Post-traumatic fistula will present with signs of orbital venous congestion such as engorged episcleral vessels and chemosis giving the appearance of a red eye, proptosis, and eyelid edema. Deficits can bilateralize if the underlying etiology lends itself to expansion or progression over time.

Orbital Apex

Trauma at the orbital apex is frequently a result of orbital fractures extending posteriorly. The presentation of orbital apex injuries differs from cavernous sinus pathology in that the maxillary branch of CNV (V_2) may be selectively spared, the optic nerve is more likely to be involved, and there is no bilateral spread of deficits with time.

Orbit

Acutely, retrobulbar hemorrhage can cause proptosis, marked extraocular motility deficits ("frozen globe"), and decreased vision. Retrobulbar hematoma is a vision-threatening emergency because the elevated intraorbital pressure creates a compartment syndrome effect, compressing the optic nerve and potentially blinding the eye. It should be treated immediately with release of the intraorbital pressure by lateral canthotomy and cantholysis performed by an emergency medicine provider or ophthalmologist.

Subacutely, orbital cellulitis can occur due to traumatic introduction of debris (bacterial and fungal etiologies should be suspected), or ascending spread of paranasal sinus flora through bony defects created by orbital fractures. A progressively swollen, red, proptotic eye with decreasing motility in the 3–12 days after orbital injury should raise suspicion for infectious cellulitis.

Extraocular Muscles

The extraocular muscles can be directly damaged by head trauma when the mechanism involves facial injury. Extraocular muscle injury can produce weakness that potentially mimics cranial nerve injuries, but muscular injuries tend to give nonspecific motility deficits because multiple muscles are usually involved. From an examination and management standpoint, it is important to distinguish between contusion and entrapment. Contusion gives a diffuse decrease in extraocular motility, often causing difficulty looking *toward* the fracture. In contrast, entrapment tethers the muscle within the orbital fracture defect, causing difficulty looking *away* from the fracture, positive forced ductions testing, nausea, and pain out of proportion to exam as the entrapped muscle becomes ischemic.

Conclusions

Traumatic neuro-ophthalmic deficits arise from injury of the afferent and/or efferent visual systems. A structured approach to assessing the afferent and efferent visual pathways can help with diagnosis of these deficits. After injury, patients should be followed closely for evolution of their deficits (worsening due to edema, hematoma expansion, or the presence of bony fragments; improvement due to edema resolution, recovery of function, or neurologic plasticity). Acute and subacute management relies upon tailoring evidence-based medicine to each trauma patient's unique situation. Long-term management can be improved by providing appropriate resources and referrals to neuro-ophthalmology and/or low-vision specialists.

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Compliance with Ethics Guidelines

Conflict of Interest Sarah M. Jacobs declares that she has no conflict of interest. Gregory P. Van Stavern has given medical-legal consultation for various companies.

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