Electrophysiological Analysis of Traumatic Optic Neuropathy and Traumatic Brain Injury Among Active Military

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Received: 21 June 2022, Manuscript No. MRCS-22-67140; **Editor assigned:** 23 June 2022, Pre QC No. MRCS-22-67140 (PQ); **Reviewed**: 04 June 2022, QC No.: MRCS-22-67140 (Q); **Revised**: 07 July 2022, Manuscript No. MRCS-22-67140(R); **Published**: 10 July 2022; DOI.: 10.4172/2572 5130.22.7(6).1000201

Abstract

Background: Traumatic Optic Neuropathy (TON) can cause persistent visual deficits and is a known sequala of Traumatic Brain Injury (TBI). Little is known regarding appropriate diagnosis, management, and treatment.

Methods: we performed a prospective cohort study with 356 active military personnel using electrophysiological Visual Evoked Potential (VEP) testing for TON in the context of known or suspected TBI. This was done with the intent to review and revise management protocol for patients who are susceptible to TON. This new VEP protocol was incorporated with kinetic and static visual field testing to uncover occult cases of TON previously missed in the current disability examination, as well as aid in evaluation of patients with borderline concussive cases that do not meet current diagnosis of mild, moderate, or severe TBI by the Veteran's Disability Exam.

Results: 80 patients were diagnosed with TON. Average age of TON patients was 37.4 years, with most patients being male. Of those patients with TON, 45% had reported TBI, whereas an additional 54% had suspected history of concussion. Patients presented with bilateral TON (65.8%, n=52), while unilateral TON cases occurred less frequently (35.4%, n=28). Visual field defects were apparent in both static and kinetic visual field testing in 54% of cases. VEP sensitivity in our study was 88%. Military parachute jumpers (paratroopers) represent the highest risk group for undiagnosed TBI and TON.

Conclusions: we recommend periodic static and kinetic visual field testing in high-risk individuals working in fields with high concussion rates. Focused collaboration for safer helmet design is imminent. By improving helmet design, we can reduce mTBI and related TON, as well as reduce costly medical care and disability payments after military discharge.

Keywords: Traumatic optic neuropathy • Visual evoked potential • Traumatic brain injury • Concussion • Disability

Background

Traumatic Optic Neuropathy (TON) has historically been viewed as a rare form of trauma induced damage to the optic nerve. While reported as only 1 per million in the general population, TON has a significantly higher prevalence among people with closed head injuries and Traumatic Brain Injury (TBI) [1]. From May 2021 to November 2021, a prospective study was performed to report undiagnosed cases of TON that were not detected with standard kinetic visual field testing in veteran disability exams [2]. The results of that study confirmed the need for both kinetic and static visual field testing to aid in the diagnosis of TON in our veteran population [2]. This present study continues the investigation into TON and role of Visual Evoked Potential (VEP) electrophysiological analysis in confirming TBI or mTBI cases in instances of head concussions that don't meet current diagnostic protocol for clinical evaluation for neurotrauma. Traumatic Optic Neuropathy (TON) is a form of optic nerve damage caused by either direct or indirect trauma to the head/orbit [1]. Indirect TON is caused by a transmission of force through the skull to the optic nerve, propagating shearing of the retinal ganglion cells [1,3]. Typical TON presentation includes some combination of decreased visual acuity, visual field defects, relative afferent pupillary defect, and chronic optic disc atrophy [1,4]. TON has been classified as a rare cause of trauma induced visual impairment but has been reported to occur in 0.5% to 5% of closed head injuries, and up to 40% to 72% of TBIs with loss of consciousness [1,3,4]. We specifically targeted the mild TBI population for this study. Traumatic brain Injury (TBI) is a spectrum of brain damage that can manifest from multiple etiologies. It is generally classified as severe, moderate, or mild with patients grouped by Glasgow coma scale score on arrival. On the more severe spectrum, diffuse axonal injury, traumatic contusions, and subdural/epidural hematomas can cause changes in intracranial pressure, early herniation, and long term neuroinflammation [5]. Orbital fractures are common in the population and globe injuries are not infrequent. These factors can alter visual field testing. Moderate TBI also causes sustained edema and inflammation with long-term cognitive and motor deficits [6]. Visual disturbances are often common in this population but clouded analysis due to clinical focus on addressing more systemic issues. On the mild spectrum, patients can have concussive and sub-concussive impacts. These findings can produce TON and long-term deficits, but due to the mild nature of the symptoms are often overlooked in the initial interval [7]. Many patients with sub-concussive injuries never get screened in a clinical setting and are more often to see medics. Having a screening tool to initiate early interventions is critical for this often-overlooked patient population.

Methods

Our protocol consisted of a comprehensive eye exam including both kinetic and static visual fields using the Humphrey Field Analyzer and electrophysiological testing with VEP on all active military personnel on terminal leave with a history of TBI and/or mTBI (head concussions) during active military service. It was presumed that these same individuals likely had many sub-concussive injuries not reported or medically evaluated. For VEP assessment, one eye was measured at a time with scalp electrodes placed over both hemispheres of the occipital region. Patients are shown a black and white checkerboard stimulus on a display with a central fixation point, at a distance between 50 cm to 150 cm away. Pattern reversal stimulus with black and white checks reversing at 2 per second (2 Hz) was viewed and recorded as N75 (N1), P100 (P1), and N135 (N2) pattern reversal latencies.

Any service member who had a history of head injury before military service was eliminated from the study. However, to aid in diagnosis and treatment, these active personnel were still evaluated for TON despite not being included in the results. Veterans who had already been discharged from the military were still tested with our new protocol but not included in the results to eliminate any possible non-military events that could have contributed to potential neurotrauma burden. Active service members with other eye pathology that could affect VEP and/or visual field testing such as glaucoma, diabetic retinopathy, multiple sclerosis, etc. were also removed from the study group. Important variables that were examined included age, sex, cause of TBI or mTBI, bilateral verse unilateral TON diagnosis, type of visual field loss, and types of VEP abnormalities.

Result

From December 1, 2021 to Feb 31, 2022, a total of 356 active military personnel were examined by referral from QTC, VES, and LHI. 79 cases of traumatic optic neuropathy were diagnosed out of the 356 veteran disability exams performed. The average age of TON patients was 37.4 years, with most patients being male. Of those patients with TON, 45% had reported TBI, whereas 54% had suspected concussion with no formal evaluation. The causes of TON were divided into blunt trauma, falls, Motor Vehicle Accidents (MVA), explosions, and paratrooper-related activities. The most common cause of TBI/mTBI resulting in TON was due to paratrooper related activities (45%), with explosives as the second most

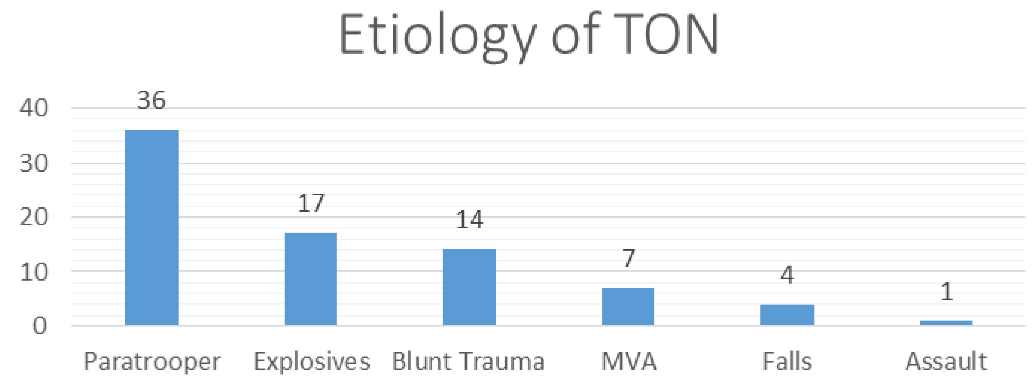

Figure 1. Causes of TON in 3-month Prospective Study. During this 3-month prospective study at the Goldsboro Eye Clinic, 79 cases of TON were identified. The various causes were classified into 5 categories: paratrooper-related events (n=36), Explosive events (n=17), blunt trauma (n=14), Motor vehicle accidents (n=7), Falls (n=4), and Assault (n=1).

Table 1. Goldsboro Eye Clinic Veteran Diagnosis Patterns of TON

Patterns of VEP AND Visual Testing						
VF results	Kinetic + Static + 43/79		Kinetic - Static + 24/79		Kinetic + Static- Dec-79	
VEP results	VEP + 36/43	VEP - Jul-43	VEP + 23/24	VEP - Jan-24	VEP + 11-Dec	VEP - 01-Dec

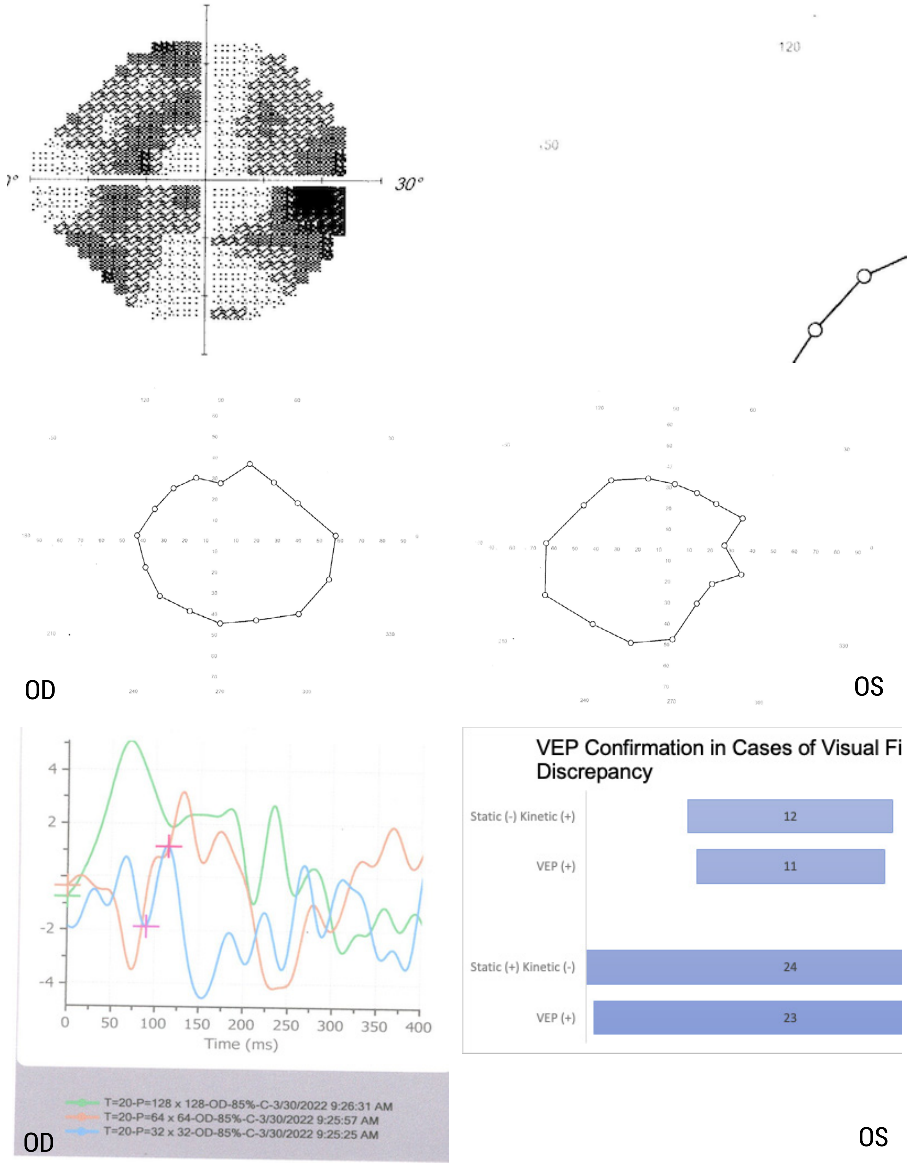

Figure 2. Visual Field and VEP testing in a case of bilateral TON. Visual field and VEP testing results of a bilateral TON case in a patient with a history of head concussion secondary to parachute jumping A) Static field-testing showing elements of bitemporal loss with nasal step B) Kinetic field testing showing superior notching (OD) and nasal notching (OS) C) VEP testing revealing bilateral abnormalities in amplitude and latency.

common activity (21.5%) (Figure 1).

Multiple patterns of VEP and visual field testing were observed among these cases, which are outlined in (Table 1). A majority of patients presented with bilateral TON (65.8%, n=52), while unilateral TON cases occurred less frequently (35.4%, n=28). Visual field defects were apparent in both static and kinetic visual field testing in 54% of cases (Figure 2). In the remaining cases, 30% demonstrated field defects only in static field testing and 15% only in kinetic field testing. VEP analysis was positive in 70 cases of TON out of a total 79 cases, with prolongation of P100 latency as the most common abnormality. A significant decrease in VEP amplitude was found in our patient cases, which is reported to be observed with optic atrophy [15]. In manifestations where static-kinetic dissociation was apparent, VEP testing provided objective confirmation of optic nerve abnormality in 92% to 95% of these cases (Figure 3). Furthermore, 83.7% of patients with undiagnosed TBI had a positive VEP testing, confirming the presence of optic nerve damage. Most importantly, it was recognized that neither VEP analysis nor static/kinetic visual field testing confirmed every TON presentation. 24 VF defects were unrecognized in kinetic field examination, while 12 VF defects were unrecognized in static field testing. Although an objective testing modality, VEP was negative in 9 cases where visual field defects were apparent, making the VEP sensitivity in our study approximately 88%. Furthermore, while most bilateral cases of TON showed marked abnormalities in VEP testing, clear differentiation in VEP testing between eyes in unilateral cases of TON was not always apparent.

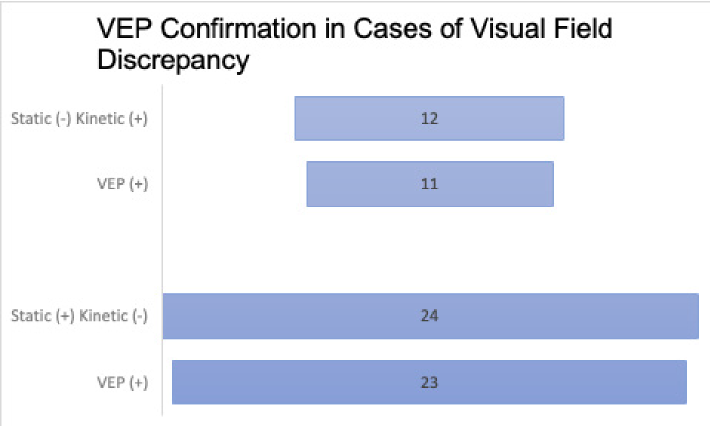

Figure 3. VEP Confirmation in Cases of Visual Field Discrepancy. During visual field testing with static and kinetic perimetry, 45% of cases resulted in statickinetic dissociation where either the kinetic or static testing was negative. VEP provided an objective analysis, confirming optic nerve injury in 92%-95% of these discrepant cases. VEP was positive in 11/12 of patients with a negative static field. VEP was positive in 23/24 cases of patients with a negative kinetic field.

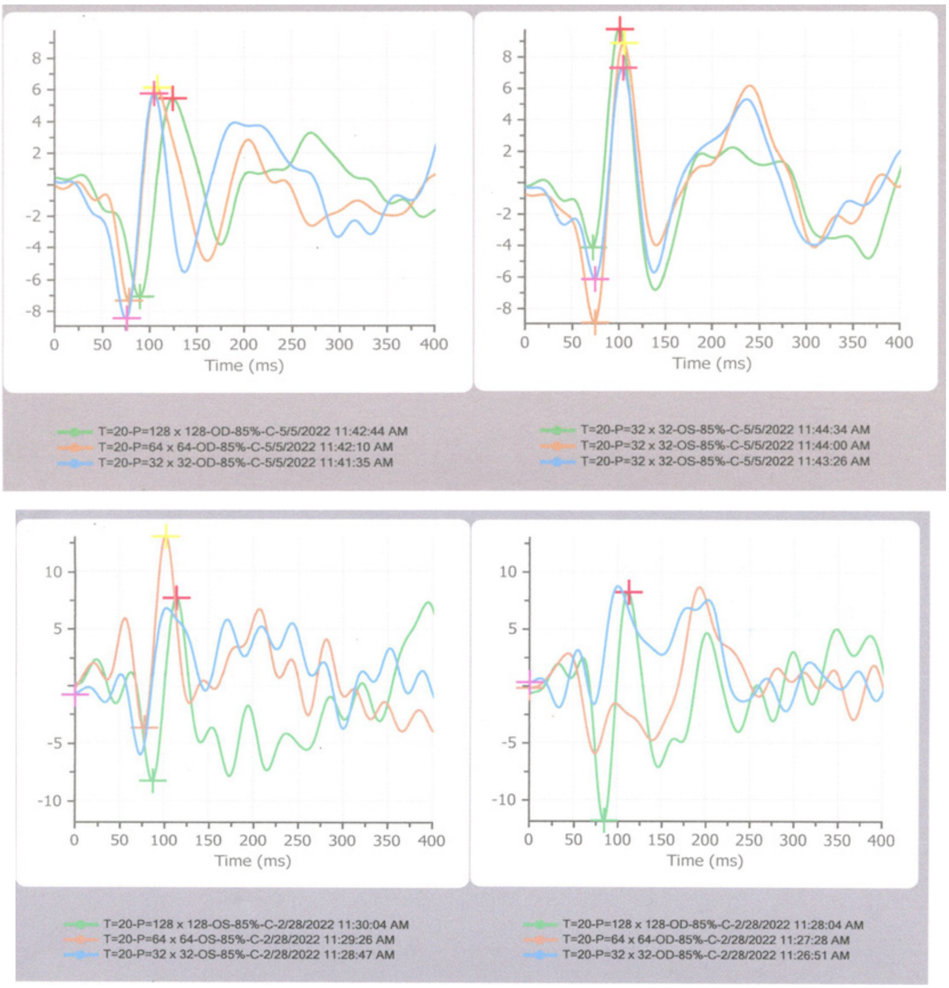

Figure 4. Comparison of VEP graph results in Unilateral TON cases. The following graphs represent VEP testing in two different unilateral TON cases. The first case (A) represents a clearly defined unilateral TON with decreased amplitude and latency seen in the right eye VEP. The second case (B) represents a case of left unilateral TON, but with VEP abnormalities seen in both eyes. Without additional corresponding visual field deficits, these VEP abnormalities are not confirmatory for TON in the right eye.

In most unilateral cases, VEP testing showed slightly abnormalities in both eyes (Figure 4). This could possibly be due to multiple reasons, as the amplitude and latency of VEP can be affected by multiple variables, including the size of the stimulus pattern and stimulus intensity, electrode placement, and scalp thickness. Latency also naturally becomes delayed with increasing age [8].

Discussion

Visual dysfunction is a common presentation after traumatic head injury. In a 2019 MSMR report among military service members, the most common visual symptoms were subjective central vision loss, convergence insufficiency, visual field loss, and accommodative dysfunction [9]. A total of 4,30,000 TBI cases have been reported by the Defense and Veterans Brain Injury Center since the year 2000, making TBI a considerable injury within the military population [9]. Additionally, this does not take into consideration sub-concussive injuries that might have been missed or poorly diagnosed. There is a clear, direct relationship between TBI/mTBI and TON. This was confirmed by a longitudinal ten year follow up study that established a 3-time increased risk of developing TON after TBI [10]. Even mild TBI can cause subtle damage to the optic nerve without widespread cortical neurodegeneration [11]. Repetitive injuries are common, likely contributing to an additive and cumulative affect over time. Although optic nerve injury is one of the most common events after TBI, nerve damage can be difficult to evaluate clinically [12]. This points to the importance of obtaining a medical history of concussion or head trauma in the evaluation of patients with unspecified visual field loss. Astute medics should direct at-risk warfighters to screening early to institute diagnosis and treatment.

The variability in TON presentation makes subtle cases easy to overlook. TON often presents with sudden temporary visual loss, but routine neurological assessment can appear normal, and may not be a sensitive tool for evaluating potential optic neuropathy. Furthermore, the cognitive and behavioral effects of mild TBI may mask more focused assessment of visual deficits delaying patients from seeking care. When TON occurs from damage to the posterior optic nerve, retinal examination will not display any gross abnormalities, due to the lack of retinal vasculature disruption. Damage to the retinal ganglion cells is also delayed, occurring 3 weeks -6 weeks post trauma, when signs of possible optic disc pallor and atrophy would first be appreciated on fundus examination [1, 13]. Deceleration injuries from motor vehicle accidents account for the primary cause (17% to 63%) of TON cases, followed by blunt trauma/ falls as the second most common cause [13]. In warfighters and paratroopers, the sustained high velocity impacts can cause micro-shearing of axonal tracts predisposing to TON. TON is associated with TBI and is more likely to occur when there is a loss of consciousness. However, as we report herein, it can occur frequently in mTBI as well.

Evaluating Optic Nerve Function

Evaluation of optic nerve function has been historically guided by visual field testing: kinetic and static visual field analysis. In the past twenty years with the advent of more affordable and efficient design, electrophysiology testing has become a valuable addition in the evaluation.

Kinetic and Static Perimetry

Visual field testing is an important tool in providing information about location of optic nerve damage and revealing visual impairments possibly unknown to patients [14]. While both kinetic and static perimetry have been shown to reliably detect visual field loss, the two tests are not equivocal [15]. Differences in visual field profiles between static and kinetic testing has long been observed and is referred to as static-kinetic dissociation [16, 17]. It has been noted in the literature that static perimetry is generally superior to kinetic in evaluating the central field of vision, while kinetic perimetry is better at evaluating the extent of the peripheral field [14, 18-21]. A 2009 comparison showed static perimetry was able to detect small paracentral scotomas while the relative kinetic perimetry remained normal. Static perimetry was 19% more sensitive for paracentral scotoma defects in this study [21]. In our patients, static perimetry was more sensitive for VF defects in Third Occipital Nerve (TON) cases, mainly in revealing para-central type scotomas. Kinetic perimetry proved useful in revealing peripheral defects that static perimetry missed. The degree of error in using these perimetry tests individually confirms the hypothesis of our earlier case report: a single visual field analysis is not adequate in the examination of visual problems resulting from head concussions. While static-kinetic dissociation may be an underlying cause to the variations in visual field testing, both static and kinetic fields are an inherently subjective testing method. Electrophysiology is an objective method, that used in conjunction with the mainly subjective presentation of TON, can confirm optic nerve damage.

Electrophysiological Testing

Ophthalmic electrophysiology analyzes the electrical signal generated in vision which involves the creation of an electrical signal generated in the retina and subsequent propagation through the optic nerve and optic tracts in the brain to the occipital lobe. There are various electrophysiological testing methods to measure this electrical signal. First the signal production in the retina is isolated with precise measured amounts of flashes of light and then compared to the produced electrical signal in the brain. The recording maps how closely the occipital lobe brain wave potential responds to visual stimulation in the retina [8, 22]. The two basic electrophysiological testing methods are the Electrogram and the VEP. In our study we focused on the use of the VEP.

Visual-evoked potential

VEPs are used to quantify the functional integrity of the visual pathways from the retina via the optic nerves, optic tracts to thalamus, projections to the visual cortices, and occipital cortical activity [22]. The VEP was initially described by Adrian in 1934 and has been used in clinical and research laboratories for almost 50 years [8]. Based on the research of Halliday in the 1970s, pattern reversal VEPs (PVEPs) are usually delayed in optic nerve demyelination. They were also the first group to report that pattern reversal VEP delays in optic nerve demyelination can occur with no sign or symptoms of optic nerve involvement [22]. VEPs provide a better assessment of the functional integrity of the optic pathways than scanning techniques such as magnetic resonance imaging (MRI), because any abnormality that affects the retina, visual pathways, or visual cortex can affect the VEP [22]. For example, meningitis or anoxia induced cortical blindness, demyelinating optic neuritis, optic atrophy, stroke, compression of the optic pathways, and retinal causes such as macular degeneration can all cause abnormal VEPs [22]. This test is designed to demonstrate alterations in optic nerve function and injuries in the anterior part of the visual pathway. Although not specific, VEP aids in detecting diseases that affect the optic nerve like optic neuropathies, glaucoma, and tumors compressing the optic nerve [22]. VEP has demonstrated more accuracy in the evaluation of pre-chiasmatic disorders.

Another application of VEP is to quantify visual system function following trauma. It is not unusual that compression of optic pathways immediately after severe trauma results in no recordable VEPs. However, VEPs may be recordable days later when inflammation subsides [22]. Interpretation of VEPs must be considered within the context of the patient's clinical appearance and information available from other tests and examinations. Therefore, VEP must be used on conjunction with clinical history and comprehensive eye examination to determine the final diagnosis. VEP can provide an objective assessment of visual field defects not yet present on automated perimetry in patients with optic neuropathies. VEP results also can predict visual recovery in TON, "with lower VEP amplitudes and longer latencies indicating worse visual acuity" [8]. While VEP is useful in detecting optic nerve dysfunction, it is not specific for determining causation.

Veteran Disability Exams

The current Veteran Disability Exams require a comprehensive eye evaluation of the veteran: visual acuity with and without best correction, intra-ocular eye pressures, and evaluation of the anterior and posterior segments of the eye. Pupil reaction to light, accommodation, muscle balance, color vision and depth perception are also evaluated. In addition, kinetic visual field testing is required. After recording all normal and abnormal findings, a nexus is established to determine any causal relationship between military service and documented eye pathology. Any claimed condition by the veteran because of his/her military service is addressed by the physician. To obtain veteran disability benefits, the examiner must demonstrate that the diagnosed medical condition is as likely as not to be caused by an in-service incident or service-connected condition. Disability payment for eligible veteran's results in a tax-free monthly payment, for which veterans could receive with 30-100% disability rating shown in (Table 2) [11].

Veteran disability examinations require kinetic field testing but lack an indication or coverage for static field testing. Our previous evaluation demonstrated a higher prevalence of TON was found among veterans with the inclusion of static visual field testing. Other objective testing such as

Table 2. Basic Rates for monthly disability payments 2021.

Disability rating for Veteran without dependents	Payment (in US $) per month
30% disability	$ 441.35
40% disability	$635.77
50% disability	$905.04
60% disability	$1,146.39
70% disability	$1,444.71
80% disability	$1,679.35
90% disability	$1,887.18
100% disability	$3,146.42

RNFL, OCT, and VEP, which are necessary for further evaluation of TON and TBI also lack coverage in disability examinations. Also, many of the study cases had subtle problems with oculomotor issues and visual tracking, which is associated with mTBI. Currently, disability ratings are limited to visual acuity and visual field calculations and do not have a clear rating system for oculomotor dysfunction.

Evaluation and Recommendation

This study demonstrates the value of VEP testing to assist in the diagnosis of TON and mTBI. By using VEP testing as well as both kinetic and static visual field testing, missed TON diagnosis can be prevented. Moreover, these tests can help establish and/or confirm the diagnosis of mTBI when combined with current screening tools. A pattern of undiagnosed TON and mTBI cases in the military population has emerged that is more common than the general population. In patients with a history of TBI and/or suspected mild TBI, we would recommend that all active service military personal and all veteran eye screening exams be amended to include VEP electrophysiological testing as well as static and kinetic visual field testing. Even if initial evaluation is negative, repeat testing over time is indicated as delayed inflammation is a known cause. This recommendation allows the strengths of all the tests to be utilized in the evaluation of highly variable outcomes. VEP testing is an excellent screening test to alert the practitioner of any variation in nerve conduction. Static perimetry has a higher sensitivity for detecting defects in the central 30°C of vision, while kinetic perimetry provides a better assessment of the periphery. Initiating the routine use of VEP testing and both perimetry testing would not significantly change the cost, time, or personnel needed in workup, but could prevent a proportion of false negative results and unidentified visual disabilities.

It is also important to anticipate that patients who have known mTBI may be at risk for complex presentation of abnormal VEP readings, as well as visual loss in either the kinetic and/or static visual fields. Some of the loss is due to cortical brain injury and other losses may be due to damage to the optic nerve. Teasing apart mechanism can aid in treatment.

Currently, the VA requires diagnosis of TBI to be made by either a neurologist, neurosurgeon, physical medicine and rehabilitation (PM and R) physicians, or psychiatrist [23]. Through electrophysiological analysis, a TBI diagnosis can be observed in a different manner. VEP analysis has potential to aid in the assessment of unclear TBI and/or mTBI cases that could otherwise be cleared neurologically prior to assessment in a clinic. We propose a future collaboration between neurologists, neurosurgeon, physiatrists, psychiatrist, and ophthalmologists in assessing TBI and TON.

Future Diagnostic Concerns

Every patient that was examined and diagnosed with TON was provided an explanation of the medical condition. Our concern was to anticipate future diagnostic potential issues. Namely, some of the visual field losses from TON could easily be interpreted as a loss from another disease. For example, it is possible that another eye care professional, who is unaware of the TON history, might diagnosis and treat the patient for normotensive type glaucoma, or optic neuropathy from an unknown cause like multiple sclerosis, etc. By informing and educating the patient about TON, a future incorrect diagnosis and/or treatment could be avoided.

Limitations and Future Research Needed

Our prospective VEP study represents only the beginning in understanding how TON is involved with TBI and mTBI cases among our military personnel. Several limitations were apparent in our study. We were restricted to only one exam allowed for each veteran. This contributed to extensive loss to follow up. We did not have access to spectral Optical Coherent Topography (SD-OCT) domain analysis and had to rely on the older stratus OCT machine. With SD-OCT testing, a more detailed study of the retinal nerve fiber layer, optic nerve head, and the ganglion cell complex could be performed and used as an objective comparison especially in cases of unilateral TON as well as additional confirmation of TON. Furthermore, we were not able to coordinate follow-up of the patient with neurology and neuro-ophthalmologists who could evaluate further with radiologic studies of CT scans and MRI testing, which would provide more evidenced based medicine in the diagnosis of TON. Therefore, initiation of treatment was limited given the protocol of the current disability evaluation. None the less, we did make recommendations for neurologic referral and further evaluation to the veteran's disability benefit.

Conclusion

We report the results of a prospective study of electrophysiological testing with VEP to confirm occult cases of TON among the active military performed as part of a disability benefit evaluation. The results of our investigation demonstrates the value of this new VEP protocol to diagnose cases of TON as well as assist in the diagnosis of TBI and mTBI in those borderline cases of head trauma. The study clearly identified military paratroopers as a high-risk military group for under reported head injuries. We would recommend periodic kinetic and static field testing especially for this military group. Finally, we would recommend further investigation into development of safer helmet design for the military paratroopers. An improved helmet design could reduce concussion events and reduce permanent brain damage to our veterans.

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Cite this article: Luke-Wold B, Electrophysiological Analysis of Traumatic Optic Neuropathy and Traumatic Brain Injury Among Active Military. Med Rep Case Stud. 2022, 07 (6),001-006.