Review

From provider to advocate: The complexities of mild traumatic brain injury prompt the evolution of provider engagement

Eric Singman 1*

- ¹ Wilmer Eye Institute @ Johns Hopkins Hospital; esingma1@jhmi.edu
- * Correspondence: esingma1@jhmi.edu; Tel.: (1+443-540-4105)

Abstract: Treating a patient with traumatic brain injury requires an interdisciplinary approach because of the pervasive, profound and protean manifestations of this condition. In this review, key aspects of the medical history and review of systems will be described in order to highlight how the role of any provider must evolve to become a better patient advocate. Although this review is written from the vantage point of a vision care provider, it is hoped that patients, caregivers and providers will recognize the need for the team approach; it truly takes a village.

Keywords: vision rehabilitation; review of systems; traumatic brain injury; concussion; patient advocacy.

1. Introduction

As we advance our understanding of the protean manifestations of mild traumatic brain injury (mTBI)] on the visual system in particular [1,2] and the entire patient in general [3-5], the vision care provider (VCP) will find it difficult to remain tightly focused on the patient's vision problems. As the VCP delves into a thorough review of systems, medications, social and medical histories, they will find that they have information that must be shared with the entire care team and that there will be times when they must serve as a patient advocate. Becoming an effective patient advocate requires skill, training and practice [6-9]. However, patients and their families clearly value advocacy on their behalf [10-12]. Furthermore, it is becoming clear that the TBI care team of the 21st century is optimally not only an interdisciplinary one [13-18], but may also be the best paradigm to reduce the high societal costs of TBI [19-22]. Notably, stakeholders have made it clear that they prefer and expect interdisciplinary care [23,24], so it is unlikely that a VCP will be able to avoid increasing levels of engagement with the TBI team. This review will annotate some of the more common systemic impacts of TBI and discuss pathways for the VCP who wants to maximally incorporate into the entire TBI team.

2. The Patient History

The VCP's approach to a patient known to have suffered mTBI starts with a history of the injury (or injuries). When the care delivered is in the outpatient setting weeks or months after the acute trauma (as is most often the case), the focus of the history might be on how the health status of the patient changed after TBI as well as the patient's trajectory of recovery. The HPI helps direct the VCP to explore those visual functions subserved by the areas of the brain documented to have been damaged. In mTBI, where

radiographically identified damage is often absent, the VCP must explore visual functions more subtly disrupted by concussion.

The patient's past medical history is also valuable because this might reveal conditions which could have an impact of the damage caused by mTBI. For example, it is known that a hypercoagulable state develops after TBI [25,26]; it seems reasonable to suggest that the presence of pre-injury coagulopathy could therefore potentiate the risk of thrombus after injury. Notably, thrombosis of the cerebral venous sinuses can lead to chronic intracranial hypertension which in turn can cause sight-threatening papilledema after TBI [27]. It should be mentioned that papilledema from intracranial hypertension can occur after even mild TBI and even in the absence of venous sinus thrombosis [28]. This highlights the duty of the VCP to recognize that common complaints in patients suffering TBI, such as headache and blurred vision, overlap with those caused by other conditions. Finally, a clear understanding of the patient's past medical history could reveal pre-morbid conditions that could impede rehabilitation. For example, it has been reported that patients with underlying Ehlers Danlos syndrome may have slower and less complete recovery after mTBI [29] and that pre-injury psychiatric migraine symptoms are risk factors for worse outcomes at 6-months after a mTBI [30].

3. The Review of Systems

An opportunity to truly familiarize the VCP with the patient's real-time status comes during the review of systems (ROS). A robust ROS cannot be overemphasized when working with concussion patients because of the wide variety of health problems experiences after brain injury. One should not assume that some other member of the TBI team fully explored the ROS; the VCP may very well be the first and only provider to identify a serious concern. The following list is undoubtedly incomplete. Our goal is to highlight the complexity of medical problems faced by patients with mTBI and touch upon some clinical connections that should not be overlooked.

3.1. General Health

Weight loss [31] and weight gain [31-33] are common after TBI. Weight loss could be associated with insufficient calories or nutrients required to effect recovery and could signal other concerns, such as depression or financial problems. Weight gain can be associated with lack of motivation to exercise [34], fatigue [35-38], insomnia [35, 39-41], and hypersomnia [42], all of which are known to occur after TBI. Weight gain can lead to secondary conditions that can directly impact the visual system, such as hypertension and diabetes.

3.2. Vision

The VCP will frequently be consulted when patients suffer mTBI because vision problems are common in this condition. Patients might report diplopia [1, 43-44], photophobia [45-48], dry eye [49,50], eye strain [51], blurred vision [2,52], visual acuity loss [53], visual field loss [2,53] and reduced color vision [53]. However, it is important to recognize that patients with mTBI often cannot articulate specifically their vision complaints and the use of symptom survey questionnaires could be valuable [54,55].

3.3. Vestibular System/Auditory

Common complaints related to the ears after TBI include reduced hearing [56,57], hyperacusis [58,59], tinnitus [57-58, 60-61], dizziness/vertigo [4,62] and otorrhea [63]. The VCP should be careful to ask patients whether their tinnitus is pulsatile, as that might suggest abnormal CSF pressure (high or low) or dehiscence of the semicircular canal. Both of these conditions can be associated with dizziness and can be overlooked. The VCP might be the only one to identify papilledema in patients with intracranial hypertension. Furthermore, the VCP has a perfect opportunity to look for nystagmus induced by sound (i.e., Tullio's phenomenon), a sign of semicircular canal dehiscence [64].

3.4. Olfactory

Anosmia or changes in sense of smell [65] and rhinorrhea [63] can occur after TBI. It is critical to ask the patient about rhinorrhea. A past history of sinus allergies does not guarantee that the post-TBI discharge is mucous. A CSF leak should be suspected, particularly when the discharge is clear, colorless and thin; CSF will test positive for Beta-2 transferrin [66]. Patients with CSF leaks often have symptoms of CSF hypotension and are at risk for a life-threatening spontaneous subdural hematoma [67] and/or cerebral infection [68].

3.5. Oral

Post-traumatic oromandibular dystonia [69], often associated with bruxism, occurs after TBI. Furthermore, it has been shown that bruxism contributes not only to post-TBI headaches [70] but is also correlated with the presence of tinnitus [71]. While dentists are perhaps most likely to identify bruxism because of secondary tooth wear [72], TBI patients might unfortunately not be guided to include oral health professionals on their care team, so specifically asking patients about bruxism could reveal a treatable and impactful diagnosis.

3.6. Cardiovascular

Orthostatic hypotension [73] has been reported to occur after TBI, and can manifest as symptoms commonly seen after TBI including dizziness, fatigue, nausea and headache. This condition can also be associated with tachycardia, and might be misinterpreted as anxiety attack; referral for a tilt-table test could resolve this situation and lead to appropriate treatment [74].

3.7. Respiratory

Sleep apnea [40,42] has been reported to develop in patients who incurred a TBI. This condition can be associated with bruxism although a recent systematic review suggests this is not well supported [75]. Sleep apnea can be associated with floppy eyelid syndrome [76] and it behooves the VCP to evaluate patients for this condition because it

can cause irritated eyes or even cornea abrasions during sleep. Notably, an association between sleep apnea and intracranial hypertension has been suggested; although the relationship between these two conditions may not be sufficient to recommend fundus examinations on every patient with sleep apnea [77], it seems reasonable for VCPs to look for papilledema in all of their sleep apnea patients.

3.8. Gastrointestinal

Nausea [4,62,78] and altered appetite [79] are frequent in the acute post-TBI period. When these problems persist, it is reasonable to look for other underlying problems associated with TBI that can precipitate nausea, e.g., migraine, vestibular dysfunction and abnormal CSF hydrodynamics.

3.9. Genitourinary/Endocrine

Patients with mTBI have been reported to develop erectile dysfunction [80] and altered menstrual patterns [81,82]. These problems can add to the emotional and/or social distress often burdening TBI patients, can interfere in family planning, and unfortunately are probably less likely to be explored. Recognizing these problems helps validate the difficult circumstances faced by TBI patients and also starts the path to their resolution. Notably, erectile dysfunction after TBI stems not only from psychological stressors; hypogonadism is common following TBI and testosterone replacement has demonstrated value [83]. Aside from the alterations in sex hormone levels, patients with TBI can also develop hypopituitarism [80,84,85].

3.10. Musculoskeletal

The biomechanics of TBI are such that cervical injuries are frequent sequelae [86]. Cervical injuries cause pain [87,88] that can interfere with sleep and range of motion. Moreover, traumatic neck pain can be associated with dizziness, visual disturbances and altered balance [89], hampering visual and vestibular rehabilitation efforts. Occipital neuralgia and other forms of cervicogenic headache can refer pain to the orbit, misdirecting diagnostic and therapeutic efforts; a high level of suspicion for these conditions followed by a referral of the patient to pain management specialists for consideration of occipital nerve blocks may provide the patient with critically needed relief [90]. It is also valuable to ask patients about whether they might have hypermobile joints, suggestive of underlying conditions such as Ehlers Danlos syndrome (EDS). Patients with EDS are more likely to suffer vertebral fractures [91]. In addition, brain injury may even unmask heretofore undiscovered diagnoses of hypermobile EDS [29,92]. When patients demonstrate hypermobility, preferably via a simple in-office evaluation of their Beighton score [93], a referral to a geneticist is advised.

3.11. Neurologic

Headache is the most common sequela of TBI [94,95]; this complaint not only encompasses generalized headache but also localized head pain and migraine [95]. Migraineurs may experience an increase in frequency, severity or duration of their migraines after concussion [96], and patients often experience their first migraine after TBI. Furthermore, there is a correlation with post-traumatic migraine, cognitive impairments and protracted recovery after TBI [97]. Migraine is one of the most persistent complaints after TBI, often lasting at least 1 year after injury [98] and causing reduced quality of life at 5 years post-injury [99]. Migraine is associated with an elevated risk of co-morbid conditions, including depression, anxiety and insomnia [100]; recognizing that these complaints are extremely common after TBI, one must wonder whether migraine perpetuates TBI symptoms. At any rate, referral of patients with postconcussion migraine to headache specialists who can reduce the burden of migraine is essential and it may be found that this shorten the duration and intensity of postconcussion syndrome. Notably, Chiari malformation, a congenital condition in which the cerebellar tonsils descend into the foramen magnum and which can remain subclinical in many patients, can become symptomatic after TBI [101]. Patient's with stereotypic post-TBI symptoms who are not improving should be explored for this condition by simply reviewing the brain imaging.

3.12. Integumentary

If the review of systems elicits a complaint of easy bruising, then further questioning of the patient and family should follow. Easy bruising can be seen with a number of conditions, including Ehlers Danlos syndrome [102] and bleeding disorders [103]. Notably these conditions may potentiate damage after TBI [29,104].

3.13.Hematologic

Hypercoagulability after TBI is well recognized and carries a risk of worse outcome [25,26,105]. Although it is unlikely that the VCP providing rehabilitative care will diagnose this problem, they should be aware that patients might be placed on anticoagulants and that could have an impact in planning ophthalmic surgical procedures.

3.14.Immunologic

There is strong evidence to support that concussion involves a sterile inflammation of the brain [106], as indicated by elevated levels of plasma cytokines in patients. Notably, elevated inflammatory markers are seen in patients with migraine as well [107], raising the question of whether the two conditions may perpetuate each other. It has also been shown that Mast cells degranulate after mTBI [108,109]. It should be mentioned that there is a condition known as mast cell activation syndrome [110,111], although there does not appear to be published studies exploring whether patients with this condition

have poorer outcomes after TBI. It seems reasonable to ask patients whose TBI symptoms are prolonged as to whether they might have symptoms of mast cell activation syndrome [111].

3.15.Infectious

There is a published report of a large number of patients with refractory postconcussion syndrome with symptoms lasting a year who secondarily tested positive for Lyme disease [112]. Although further study on this topic is clearly needed, it seems reasonable to explore a diagnosis of Lyme disease in patients with chronic postconcussion syndrome, particularly in areas where Lyme disease is endemic.

3.16.Psychiatric

Traumatic brain injury has been consistently demonstrated to cause dementia [113], cognitive deficits [114], anxiety and depression [115,116]. These changes can be protracted or even permanently disabling. The VCP should question every TBI patient to ensure that they have had a neuropsychological assessment. Those patients for whom this has not been scheduled should be strongly encouraged to seek such an evaluation.

4. Medications & Social History

There are many prescription medications offered to patients which cause side-effects mimicking complaints commonly reported after TBI, such as dizziness, somnolence or nausea. The VCP should take note of a patient's medication and discuss with the patient whether any TBI symptoms worsened after any particular medication was initiated. A social history is also critically important to determine how a patient's habits and social support structure might impact recovery. For example, it has been reported that perceived social support [117] and early return to exercise [118] may be salutary after mild TBI, while TBI may be a risk factor for problem gambling [119] and alcohol abuse [120]. A history of TBI is significantly more prevalent among the homeless [121] and poor [122]. It is likely that TBI causes a downward social drift, since patients often cannot work and become isolated because of their psychiatric conditions and substance abuse. VCPs and all health care providers must recognize that poverty may be the most deleterious sequela of TBI and that poverty reduced overall health and life expectancy [123]. For this reason, the VCP must determine whether the TBI has access to adequate resources and to guide patients to social work professionals if the patients do not have such access.

5. The Post-examination Conversation

The final portion of the VCP visit involves a discussion with the patient concerning the findings of the vision examination and how those findings can guide therapeutic pathways. Like every provider who treats patients with TBI, the VCP will often need to refer patients to members of the TBI-treatment team who might not already have been recruited and to facilitate communication of rehabilitative plans. The value of including a patient's significant social supporters in these conversations cannot be overstated [124]. For patients with mTBI, the main thrust of rehabilitation will usually concern lingering visuomotor problems. Because the VCP has explored the patient's circumstances, such as availability of transportation, insurance coverage, tolerance for orthoptic exercises and distance to a practitioner, the VCP can help the patient determine whether vision rehabilitation should commence or be held in abeyance until other complaints are relieved, as well as how best to balance in-office and at-home vision rehabilitation venues [125,126].

6. Patient Advocacy

The VCP complements the team of specialties demonstrated as necessary to support TBI patients, including neurology, neuropsychology, neurosurgery, pain management, neuro-otology, dentistry, physiatry and social service professionals. Like every other member of this team, the vision care provider is in a unique position to clarify the nexuses between patients' complaints that are specialty-specific with those that are non-specialtyspecific and ensure these points are adequately communicated to other members of the care team and patients. The result will be that all stakeholders have the situational awareness to make optimal informed decisions. How far the VCP goes is up to the individual provider. At the very least, every provider should ensure that their findings and suggestions are distributed to the TBI care team. Providers should also help identify and even recruit (via referral) experts that might not yet be on the TBI care team. Optimally, any provider of the care team will want to create an atmosphere of advocacy for the patient. Because TBI patients often have such complex situations, they may not be the best person to serve as their own navigator, although they must be included in every decision. When possible, guiding a family member to serve as an advocate can be helpful and there are a number of resources to help this process (for example, [127]. Finally, it must be mentioned that there are professional patient advocates who are well trained, follow a code of ethics and carry professional liability insurance; these are usually healthcare professionals who have transitioned into patient advocacy. Although these professionals might not specialize in patients with TBI, the learning curve would likely be much shorter for them should a member of the TBI team want to serve as a mentor.

5. Conclusions

TBI recovery can last months to years. It is likely that the VCP will grow very familiar with patients and their supporters during this difficult period in a patient's life. An indepth and broad understanding of the medical and social ramifications of TBI should

encourage caregivers to actualize the value of their interactions and lead the way toward the best outcomes.

Funding: This research received no external funding

Acknowledgments: The author acknowledges with gratitude the patients who sought care and guidance from the Wilmer Clinic for Vision after Brain Injury at Johns Hopkins Hospital.

Conflicts of Interest: The author declares no conflict of interest.

References

- 1. Barnett BP, and Singman EL. Vision concerns after mild traumatic brain injury. Curr Treat Options Neurol. 2015;17(2):329.
- 2. Merezhinskaya N, Mallia RK, Park D, Bryden DW, Mathur K, and Barker FM, 2nd. Visual Deficits and Dysfunctions Associated with Traumatic Brain Injury: A Systematic Review and Meta-analysis. *Optom Vis Sci.* **2019**;96(8):542-55.
- 3. Robba C, Bonatti G, Pelosi P, and Citerio G. Extracranial complications after traumatic brain injury: targeting the brain and the body. *Curr Opin Crit Care*. **2020**;26(2):137-46.
- 4. Chendrasekhar A. Persistent symptoms in mild pediatric traumatic brain injury. *Pediatric Health Med Ther.* **2019**;10:57-60.
- 5. Gaddam SS, Buell T, and Robertson CS. Systemic manifestations of traumatic brain injury. *Handb Clin Neurol.* **2015**;127:205-18.
- 6. Bernard C, Soklaridis S, Paton M, Fung K, Fefergrad M, Andermann L, et al. Family physicians and health advocacy: Is it really a difficult fit? *Can Fam Physician*. **2019**;65(7):491-6.
- 7. Hoepfer M. Becoming an advocate for the elderly. *Pa Med.* **1995**;98(11):24-6.
- 8. Martin LT, Schonlau M, Haas A, Derose KP, Rosenfeld L, Buka SL, et al. Patient activation and advocacy: which literacy skills matter most? *J Health Commun.* **2011**;16 Suppl 3:177-90.
- 9. Radder DLM, de Vries NM, Riksen NP, Diamond SJ, Gross D, Gold DR, et al. Multidisciplinary care for people with Parkinson's disease: the new kids on the block! *Expert Rev Neurother*. **2019**;19(2):145-57.
- 10. Hemphill R, Forsythe LP, Heckert AL, Amolegbe A, Maurer M, Carman KL, et al. What motivates patients and caregivers to engage in health research and how engagement affects their lives: Qualitative survey findings. *Health Expect.* **2020**;23(2):328-36.
- 11. Dulay M, Bowen JL, Weppner WG, Eastburn A, Poppe AP, Spanos P, et al. Interprofessional population health advocacy: Developing and implementing a panel management curriculum in five Veterans Administration primary care practices. *J Interprof Care*. **2018**:1-11.
- 12. Addario BJ, Fadich A, Fox J, Krebs L, Maskens D, Oliver K, et al. Patient value: Perspectives from the advocacy community. *Health Expect.* **2018**;21(1):57-63.
- 13. Moller MC, Lexell J, and Wilbe Ramsay K. Effectiveness of specialized rehabilitation after mild traumatic brain injury: A systematic review and meta-analysis. *J Rehabil Med.* **2021**;53(2):jrm00149.
- 14. Marklund N, Bellander BM, Godbolt AK, Levin H, McCrory P, and Thelin EP. Treatments and rehabilitation in the acute and chronic state of traumatic brain injury. *J Intern Med.* **2019**;285(6):608-23.
- 15. Poncet F, Swaine B, Migeot H, Lamoureux J, Picq C, and Pradat P. Effectiveness of a multidisciplinary rehabilitation program for persons with acquired brain injury and executive dysfunction. *Disabil Rehabil.* **2018**;40(13):1569-83.
- 16. Naess HL, Vikane E, Wehling EI, Skouen JS, Bell RF, and Johnsen LG. Effect of Early Interdisciplinary Rehabilitation for Trauma Patients: A Systematic Review. *Arch Rehabil Res Clin Transl.* **2020**;2(4):100070.
- 17. DeGraba TJ, Williams K, Koffman R, Bell JL, Pettit W, Kelly JP, et al. Efficacy of an Interdisciplinary Intensive Outpatient Program in Treating Combat-Related Traumatic Brain Injury and Psychological Health Conditions. *Front Neurol*. **2020**;11:580182.
- 18. Janak JC, Cooper DB, Bowles AO, Alamgir AH, Cooper SP, Gabriel KP, et al. Completion of Multidisciplinary Treatment for Persistent Postconcussive Symptoms Is Associated With Reduced Symptom Burden. *J Head Trauma Rehabil.* **2017**;32(1):1-15.
- 19. Miller GF, DePadilla L, and Xu L. Costs of Nonfatal Traumatic Brain Injury in the United States, 2016. *Med Care*. 2021. DOI: 10.1097/mlr. 0000000000001511.
- 20. Rubin R. Traumatic Brain Injury Hospital Stays Are Longer, More Costly. JAMA. 2020;323(20):1998.
- 21. Peterson C, Xu L, and Barnett SBL. Average lost work productivity due to non-fatal injuries by type in the USA. *Inj Prev.* **2020**. doi: 10.1136/injuryprev-2019-043607.
- 22. Frick KD, and Singman EL. Cost of Military Eye Injury and Vision Impairment Related to Traumatic Brain Injury: 2001-2017. *Mil Med.* **2019**;184(5-6):e338-e43.
- 23. Lannin NA, Coulter M, Laver K, Hyett N, Ratcliffe J, Holland AE, et al. Public perspectives on acquired brain injury rehabilitation and components of care: A Citizens' Jury. *Health Expect.* **2020**. doi.org/10.1111/hex.13176.

- 24. The Management of Concussion-mild Traumatic Brain Injury Working Group. In: VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF CONCUSSION-MILD TRAUMATIC BRAIN INJURY. 2016. www.healthquality.va.gov/guidelines/rehab/mtbi/mtbicpgfullcpg50821816.pdf. Accessed March 16, 2021.
- 25. Kumar MA. Coagulopathy associated with traumatic brain injury. Curr Neurol Neurosci Rep. 2013;13(11):391.
- 26. Zhang J, Zhang F, and Dong JF. Coagulopathy induced by traumatic brain injury: systemic manifestation of a localized injury. *Blood.* **2018**;131(18):2001-6.
- 27. Zabalo San Juan G, Vazquez Miguez A, Zazpe Cenoz I, Casajus Ortega A, Garcia Campos M, de Frutos Marcos D, et al. Intracranial hypertension caused by superior sagittal sinus stenosis secondary to a depressed skull fracture: Case report and review of the literature. *Neurocirugia* (Astur). **2019**;30(5):243-9.
- 28. Haider MN, Leddy JJ, Hinds AL, Aronoff N, Rein D, Poulsen D, et al. Intracranial pressure changes after mild traumatic brain injury: a systematic review. *Brain Inj.* **2018**;32(7):809-15.
- 29. Gami A, and Singman EL. Underlying Ehlers-Danlos syndrome discovered during neuro-ophthalmic evaluation of concussion patients: a case series. *BMC Ophthalmol.* **2019**;19(1):159.
- 30. Yue JK, Cnossen MC, Winkler EA, Deng H, Phelps RRL, Coss NA, et al. Pre-injury Comorbidities Are Associated With Functional Impairment and Post-concussive Symptoms at 3- and 6-Months After Mild Traumatic Brain Injury: A TRACK-TBI Study. *Front Neurol.* **2019**;10:343.
- 31. Crenn P, Hamchaoui S, Bourget-Massari A, Hanachi M, Melchior JC, and Azouvi P. Changes in weight after traumatic brain injury in adult patients: a longitudinal study. *Clin Nutr.* **2014**;33(2):348-53.
- 32. Aadal L, Mortensen J, and Nielsen JF. Weight reduction after severe brain injury: a challenge during the rehabilitation course. *J Neurosci Nurs.* **2015**;47(2):85-90.
- 33. Jourdan C, Brugel D, Hubeaux K, Toure H, Laurent-Vannier A, and Chevignard M. Weight gain after childhood traumatic brain injury: a matter of concern. *Dev Med Child Neurol.* **2012**;54(7):624-8.
- 34. Pinto SM, Newman MA, and Hirsch MA. Perceived Barriers to Exercise in Adults with Traumatic Brain Injury Vary by Age. *J Funct Morphol Kinesiol.* **2018**;3(3).
- 35. van Markus-Doornbosch F, Peeters E, van der Pas S, Vlieland TV, and Meesters J. Physical activity after mild traumatic brain injury: What are the relationships with fatigue and sleep quality? *Eur J Paediatr Neurol.* **2019**;23(1):53-60.
- 36. Cooksley R, Maguire E, Lannin NA, Unsworth CA, Farquhar M, Galea C, et al. Persistent symptoms and activity changes three months after mild traumatic brain injury. *Aust Occup Ther J.* **2018**;65(3):168-75.
- 37. Dwyer B, and Katz DI. Postconcussion syndrome. Handb Clin Neurol. 2018;158:163-78.
- 38. Ewing-Cobbs L, Cox CS, Jr., Clark AE, Holubkov R, and Keenan HT. Persistent Postconcussion Symptoms After Injury. *Pediatrics*. **2018**;142(5).
- 39. Raikes AC, Athey A, Alfonso-Miller P, Killgore WDS, and Grandner MA. Insomnia and daytime sleepiness: risk factors for sports-related concussion. *Sleep Med.* **2019**;58:66-74.
- 40. Lu LH, Reid MW, Cooper DB, and Kennedy JE. Sleep problems contribute to post-concussive symptoms in service members with a history of mild traumatic brain injury without posttraumatic stress disorder or major depressive disorder. *NeuroRehabilitation*. **2019**;44(4):511-21.
- 41. Tham SW, Aaron RV, and Palermo TM. The role of sleep deficiency in the trajectory of postconcussive symptoms in adolescents. *Brain Inj.* **2019**;33(11):1413-9.
- 42. Walker JM, James NT, Campbell H, Wilson SH, Churchill S, and Weaver LK. Sleep assessments for a mild traumatic brain injury trial in a military population. *Undersea Hyperb Med.* **2016**;43(5):549-66.
- 43. Doble JE, Feinberg DL, Rosner MS, and Rosner AJ. Identification of binocular vision dysfunction (vertical heterophoria) in traumatic brain injury patients and effects of individualized prismatic spectacle lenses in the treatment of postconcussive symptoms: a retrospective analysis. *PM R.* **2010**;2(4):244-53.
- 44. Tannen B, Good K, Ciuffreda KJ, and Moore KJ. Prevalence of esophoria in concussed patients. J Optom. 2019;12(1):64-8.
- 45. Burstein R, Noseda R, and Fulton AB. Neurobiology of Photophobia. J Neuroophthalmol. 2019;39(1):94-102.
- 46. Clark J, Hasselfeld K, Bigsby K, and Divine J. Colored Glasses to Mitigate Photophobia Symptoms Posttraumatic Brain Injury. *J Athl Train*. **2017**;52(8):725-9.
- 47. Mares C, Dagher JH, and Harissi-Dagher M. Narrative Review of the Pathophysiology of Headaches and Photosensitivity in Mild Traumatic Brain Injury and Concussion. *Can J Neurol Sci.* **2019**;46(1):14-22.
- 48. Truong JQ, Ciuffreda KJ, Han MH, and Suchoff IB. Photosensitivity in mild traumatic brain injury (mTBI): a retrospective analysis. *Brain Inj.* **2014**;28(10):1283-7.
- 49. Lee CJ, Felix ER, Levitt RC, Eddy C, Vanner EA, Feuer WJ, et al. Traumatic brain injury, dry eye and comorbid pain diagnoses in US veterans. *Br J Ophthalmol.* **2018**;102(5):667-73.
- 50. Cockerham GC, Lemke S, Glynn-Milley C, Zumhagen L, and Cockerham KP. Visual performance and the ocular surface in traumatic brain injury. *Ocul Surf.* **2013**;11(1):25-34.
- 51. Schmidtmann G, Ruiz T, Reynaud A, Spiegel DP, Lague-Beauvais M, Hess RF, et al. Sensitivity to Binocular Disparity is Reduced by Mild Traumatic Brain Injury. *Invest Ophthalmol Vis Sci.* **2017**;58(5):2630-5.

- 52. Matuseviciene G, Johansson J, Moller M, Godbolt AK, Pansell T, and Deboussard CN. Longitudinal changes in oculomotor function in young adults with mild traumatic brain injury in Sweden: an exploratory prospective observational study. *BMJ Open.* **2018**;8(2):e018734.
- 53. Singman EL, Daphalapurkar N, White H, Nguyen TD, Panghat L, Chang J, et al. Indirect traumatic optic neuropathy. *Mil Med Res.* **2016**;3:2.
- 54. Laukkanen H, Scheiman M, and Hayes JR. Brain Injury Vision Symptom Survey (BIVSS) Questionnaire. *Optom Vis Sci.* **2017**;94(1):43-50.
- 55. Berthold-Lindstedt M, Johansson J, Ygge J, and Borg K. How to assess visual function in acquired brain injury-Asking is not enough. *Brain Behav.* **2021**;11(2):e01958.
- 56. Santhanam P, Meehan A, Orrison WW, Wilson SH, Oakes TR, and Weaver LK. Central auditory processing disorders after mild traumatic brain injury. *Undersea Hyperb Med.* **2019**;46(3):261-9.
- 57. Meehan A, Hebert D, Deru K, and Weaver LK. Hidden hearing deficits in military service members with persistent post concussive symptoms. *Undersea Hyperb Med.* **2019**;46(3):251-60.
- 58. Knoll RM, Herman SD, Lubner RJ, Babu AN, Wong K, Sethi RKV, et al. Patient-reported auditory handicap measures following mild traumatic brain injury. *Laryngoscope*. **2019**. Mar;130(3):761-767. doi: 10.1002/lary.28034.
- 59. Assi H, Moore RD, Ellemberg D, and Hebert S. Sensitivity to sounds in sport-related concussed athletes: a new clinical presentation of hyperacusis. *Sci Rep.* **2018**;8(1):9921.
- 60. Chorney SR, Suryadevara AC, and Nicholas BD. Audiovestibular symptoms as predictors of prolonged sports-related concussion among NCAA athletes. *Laryngoscope*. **2017**;127(12):2850-3.
- 61. Karch SJ, Capo-Aponte JE, McIlwain DS, Lo M, Krishnamurti S, Staton RN, et al. Hearing Loss and Tinnitus in Military Personnel with Deployment-Related Mild Traumatic Brain Injury. *US Army Med Dep J.* **2016**(3-16):52-63.
- 62. Langevin P, Fait P, Fremont P, and Roy JS. Cervicovestibular rehabilitation in adult with mild traumatic brain injury: a randomised controlled trial protocol. *BMC Sports Sci Med Rehabil.* **2019**;11:25.
- 63. Amin Z, Sayuti R, Kahairi A, Islah W, and Ahmad R. Head injury with temporal bone fracture: one year review of case incidence, causes, clinical features and outcome. *Med J Malaysia*. **2008**;63(5):373-6.
- 64. Philip A, Mammen MD, Lepcha A, and Alex A. Posterior semicircular canal dehiscence: a diagnostic and surgical conundrum. *BMJ Case Rep.* **2019**;12(7).
- 65. Schofield PW, and Doty RL. The influence of head injury on olfactory and gustatory function. *Handb Clin Neurol.* **2019**;164:409-29
- 66. Oakley GM, Alt JA, Schlosser RJ, Harvey RJ, and Orlandi RR. Diagnosis of cerebrospinal fluid rhinorrhea: an evidence-based review with recommendations. *Int Forum Allergy Rhinol.* **2016**;6(1):8-16.
- 67. Williams JR, Buckley R, Oushy S, Ruzevick J, and Chesnut RM. Reversible, Position-Dependent Midbrain Compression in a Patient with Spontaneous Intracranial Hypotension. *World Neurosurg.* **2019**;130:293-7.
- 68. Karampekios S, and Hesselink J. Cerebral infections. Eur Radiol. 2005;15(3):485-93.
- 69. Pedemonte C, Perez Gutierrez H, Gonzalez E, Vargas I, and Lazo D. Use of onabotulinumtoxinA in post-traumatic oromandibular dystonia. *J Oral Maxillofac Surg.* **2015**;73(1):152-7.
- 70. Suzuki Y, Arbour C, Khoury S, Giguere JF, Denis R, De Beaumont L, et al. Does Sleep Bruxism Contribute to Headache-Related Disability After Mild Traumatic Brain Injury? A Case-Control Study. *J Oral Facial Pain Headache*. **2017**;31(4):306-12.
- 71. Michiels S, Harrison S, Vesala M, and Schlee W. The Presence of Physical Symptoms in Patients With Tinnitus: International Web-Based Survey. *Interact J Med Res.* **2019**;8(3):e14519.
- 72. Korkut B, Tagtekin D, Murat N, and Yanikoglu F. Clinical Quantitative Evaluation of Tooth Wear: A 4-year Longitudinal Study. *Oral Health Prev Dent*. **2020**;18(1):719-29.
- 73. Miranda NA, Boris JR, Kouvel KM, and Stiles L. Activity and Exercise Intolerance After Concussion: Identification and Management of Postural Orthostatic Tachycardia Syndrome. *J Neurol Phys Ther.* **2018**;42(3):163-71.
- 74. Cheshire WP, Jr., and Goldstein DS. Autonomic uprising: the tilt table test in autonomic medicine. *Clin Auton Res.* **2019**;29(2):215-30.
- 75. da Costa Lopes AJ, Cunha TCA, Monteiro MCM, Serra-Negra JM, Cabral LC, and Junior PCS. Is there an association between sleep bruxism and obstructive sleep apnea syndrome? A systematic review. *Sleep Breath.* **2020**;24(3):913-21.
- 76. Cristescu TR, and Mihaltan FD. Ocular pathology associated with obstructive sleep apnea syndrome. *Rom J Ophthalmol*. **2020**;64(3):261-8.
- 77. Farahvash A, and Micieli JA. Neuro-Ophthalmological Manifestations of Obstructive Sleep Apnea: Current Perspectives. *Eye Brain*. **2020**;12:61-71.
- 78. Mott TF, McConnon ML, and Rieger BP. Subacute to chronic mild traumatic brain injury. *Am Fam Physician*. **2012**;86(11):1045-51.
- 79. Brickell TA, Lippa SM, French LM, Kennedy JE, Bailie JM, and Lange RT. Female Service Members and Symptom Reporting after Combat and Non-Combat-Related Mild Traumatic *Brain Injury*. *J Neurotrauma*. **2017**;34(2):300-12.
- 80. Grashow R, Weisskopf MG, Miller KK, Nathan DM, Zafonte R, Speizer FE, et al. Association of Concussion Symptoms With Testosterone Levels and Erectile Dysfunction in Former Professional US-Style Football Players. *JAMA Neurol.* **2019**. Aug 26;76(12):1428–38. doi: 10.1001/jamaneurol.2019.2664.
- 81. Moreno MA. New Updates on Concussions in Girls and Menstrual Patterns. JAMA Pediatr. 2017;171(9):924.

- 82. Snook ML, Henry LC, Sanfilippo JS, Zeleznik AJ, and Kontos AP. Association of Concussion With Abnormal Menstrual Patterns in Adolescent and Young Women. *JAMA Pediatr.* **2017**;171(9):879-86.
- 83. Ripley DL, Gerber D, Pretz C, Weintraub AH, and Wierman ME. Testosterone replacement in hypogonadal men during inpatient rehabilitation following traumatic brain injury: Results from a double-blind, placebo-controlled clinical pilot study. *NeuroRehabilitation*. **2020**;46(3):355-68.
- 84. Dubourg J, and Messerer M. Sports-related chronic repetitive head trauma as a cause of pituitary dysfunction. *Neurosurg Focus*. **2011**;31(5):E2.
- 85. Schneider M, Schneider HJ, Yassouridis A, Saller B, von Rosen F, and Stalla GK. Predictors of anterior pituitary insufficiency after traumatic brain injury. *Clin Endocrinol (Oxf)*. **2008**;68(2):206-12.
- 86. Gil C, and Decq P. How similar are whiplash and mild traumatic brain injury? A systematic review. *Neurochirurgie*. **2021**. Jan 30:S0028-3770(21)00026-6. doi: 10.1016/j.neuchi.2021.01.016.
- 87. Ducic I, Sinkin JC, and Crutchfield KE. Interdisciplinary treatment of post-concussion and post-traumatic headaches. *Microsurgery*. **2015**;35(8):603-7.
- 88. Zaremski JL, Herman DC, Clugston JR, Hurley RW, and Ahn AH. Occipital neuralgia as a sequela of sports concussion: a case series and review of the literature. *Curr Sports Med Rep.* **2015**;14(1):16-9.
- 89. Treleaven J. Dizziness, Unsteadiness, Visual Disturbances, and Sensorimotor Control in Traumatic Neck Pain. *J Orthop Sports Phys Ther.* **2017**;47(7):492-502.
- 90. Williams KA, Lawson RM, Perurena OH, and Coppin JD. Management of Chronic Migraine and Occipital Neuralgia in Post 9/11 Combat Veterans. *Mil Med.* **2019**;184(7-8):e207-e11.
- 91. Mazziotti G, Dordoni C, Doga M, Galderisi F, Venturini M, Calzavara-Pinton P, et al. High prevalence of radiological vertebral fractures in adult patients with Ehlers-Danlos syndrome. *Bone*. **2016**;84:88-92.
- 92. Hamonet C, Fredy D, Lefevre JH, Bourgeois-Gironde S, and Zeitoun JD. Brain injury unmasking Ehlers-Danlos syndromes after trauma: the fiber print. *Orphanet J Rare Dis.* **2016**;11:45.
- 93. Armstrong R, and Greig DM. The Beighton score as a predictor of Brighton criteria in sport and dance. *Phys Ther Sport*. **2018**;32:145-54.
- 94. Ofoghi Z, Dewey D, and Barlow KM. A systematic review of structural and functional imaging correlates of headache or pain following mild traumatic brain injury. *J Neurotrauma*. **2019**. Apr 1;37(7):907-923. doi: 10.1089/neu.2019.6750.
- 95. Ashina H, Porreca F, Anderson T, Amin FM, Ashina M, Schytz HW, et al. Post-traumatic headache: epidemiology and pathophysiological insights. *Nat Rev Neurol.* **2019**;15(10):607-17.
- 96. Dwyer B. Posttraumatic Headache. Semin Neurol. 2018;38(6):619-26.
- 97. Kontos AP, Elbin RJ, Lau B, Simensky S, Freund B, French J, et al. Posttraumatic migraine as a predictor of recovery and cognitive impairment after sport-related concussion. *Am J Sports Med.* **2013**;41(7):1497-504.
- 98. Hoffman JM, Lucas S, Dikmen S, and Temkin N. Clinical Perspectives on Headache After Traumatic Brain Injury. *PM R*. **2020**;12(10):967-74.
- 99. Stacey A, Lucas S, Dikmen S, Temkin N, Bell KR, Brown A, et al. Natural History of Headache Five Years after Traumatic Brain Injury. *J Neurotrauma*. **2017**;34(8):1558-64.
- 100. Buse DC, Reed ML, Fanning KM, Bostic R, Dodick DW, Schwedt TJ, et al. Comorbid and co-occurring conditions in migraine and associated risk of increasing headache pain intensity and headache frequency: results of the migraine in America symptoms and treatment (MAST) study. *J Headache Pain*. **2020**;21(1):23.
- 101. Spencer R, and Leach P. Asymptomatic Chiari Type I malformation: should patients be advised against participation in contact sports? *Br J Neurosurg.* **2017**;31(4):415-21.
- 102. Malfait F, Castori M, Francomano CA, Giunta C, Kosho T, and Byers PH. The Ehlers-Danlos syndromes. *Nat Rev Dis Primers*. 2020;6(1):64.
- 103. Ballas M, and Kraut EH. Bleeding and bruising: a diagnostic work-up. Am Fam Physician. 2008;77(8):1117-24.
- 104. Nassiri F, Badhiwala JH, Witiw CD, Mansouri A, Davidson B, Almenawer SA, et al. The clinical significance of isolated traumatic subarachnoid hemorrhage in mild traumatic brain injury: A meta-analysis. *J Trauma Acute Care Surg.* **2017**;83(4):725-31.
- 105. Maegele M. Coagulopathy after traumatic brain injury: incidence, pathogenesis, and treatment options. *Transfusion*. **2013**;53 Suppl 1:28S-37S.
- 106. Vedantam A, Brennan J, Levin HS, McCarthy JJ, Dash PK, Redell JB, et al. Early versus Late Profiles of Inflammatory Cytokines after Mild Traumatic Brain Injury and Their Association with Neuropsychological Outcomes. *J Neurotrauma*. **2021**;38(1):53-62.
- 107. Togha M, Razeghi Jahromi S, Ghorbani Z, Ghaemi A, and Rafiee P. Evaluation of Inflammatory State in Migraineurs: A Casecontrol Study. *Iran J Allergy Asthma Immunol.* **2020**;19(S1):83-90.
- 108. Kempuraj D, Selvakumar GP, Thangavel R, Ahmed ME, Zaheer S, Raikwar SP, et al. Mast Cell Activation in Brain Injury, Stress, and Post-traumatic Stress Disorder and Alzheimer's Disease Pathogenesis. *Front Neurosci.* **2017**;11:703.
- 109. Levy D, Edut S, Baraz-Goldstein R, Rubovitch V, Defrin R, Bree D, et al. Responses of dural mast cells in concussive and blast models of mild traumatic brain injury in mice: Potential implications for post-traumatic headache. *Cephalalgia*. 2016;36(10):915-23.
- 110. Giannetti A, Filice E, Caffarelli C, Ricci G, and Pession A. Mast Cell Activation Disorders. Medicina (Kaunas). 2021;57(2).
- 111. Matito A, Escribese MM, Longo N, Mayorga C, Luengo-Sanchez O, Perez-Gordo M, et al. Clinical Approach to Mast Cell Activation Syndromes: A Practical Overview. *J Investig Allergol Clin Immunol.* **2021**:0. doi: 10.18176/jiaci.0675.

- 112. Azzolino S, Zaman R, Hankir A, and Carrick FR. The prevalence of Lyme disease and associated co-infections in people with a chronic post-concussive syndrome. *Psychiatr Danub*. **2019**;31(Suppl 3):299-307.
- 113. Donovan J, Cancelliere C, and Cassidy JD. Summary of the findings of the International Collaboration on Mild Traumatic Brain Injury Prognosis. *Chiropr Man Therap.* **2014**;22(1):38.
- 114. Filley CM, and Kelly JP. White Matter and Cognition in Traumatic Brain Injury. J Alzheimers Dis. 2018;65(2):345-62.
- 115. McAllister TW, and Wall R. Neuropsychiatry of sport-related concussion. *Handb Clin Neurol.* **2018**;158:153-62.
- 116. Auxemery Y. Post-traumatic psychiatric disorders: PTSD is not the only diagnosis. Presse Med. 2018;47(5):423-30.
- 117. Zeng EQ, Zeng BQ, Tian JL, Du B, Tian XB, and Chen H. Perceived Social Support and Its Impact on Mental Fatigue in Patients with Mild Traumatic Brain Injury. *Balkan Med J.* **2016**;33(2):152-7.
- 118. Mychasiuk R, Hehar H, Ma I, Candy S, and Esser MJ. Reducing the time interval between concussion and voluntary exercise restores motor impairment, short-term memory, and alterations to gene expression. *Eur J Neurosci.* **2016**;44(7):2407-17.
- 119. Bhatti JA, Thiruchelvam D, and Redelmeier DA. Traumatic brain injury as an independent risk factor for problem gambling: a matched case-control study. *Soc Psychiatry Psychiatr Epidemiol.* **2019**;54(4):517-23.
- 120. Hanson KL, Schiehser DM, Clark AL, Sorg SF, Kim RT, Jacobson MW, et al. Problem alcohol use in veterans with mild traumatic brain injury: Associations with cognitive performance and psychiatric symptoms. *J Clin Exp Neuropsychol*. **2016**;38(10):1115-30.
- 121. Young JT, and Hughes N. Traumatic brain injury and homelessness: from prevalence to prevention. *Lancet Public Health*. **2020**;5(1):e4-e5.
- 122. Kisser J, Waldstein SR, Evans MK, and Zonderman AB. Lifetime prevalence of traumatic brain injury in a demographically diverse community sample. *Brain Inj.* **2017**;31(5):620-3.
- 123. Egen O, Beatty K, Blackley DJ, Brown K, and Wykoff R. Health and Social Conditions of the Poorest Versus Wealthiest Counties in the United States. Am J Public Health. 2017;107(1):130-5.
- 124. Sansonetti D, Nicks RJ, and Unsworth C. Barriers and enablers to aligning rehabilitation goals to patient life roles following acquired brain injury. *Aust Occup Ther J.* **2018**;65(6):512-22.
- 125. Aletaha M, Daneshvar F, Mosallaei M, Bagheri A, and Khalili MR. Comparison of Three Vision Therapy Approaches for Convergence Insufficiency. *J Ophthalmic Vis Res.* **2018**;13(3):307-14.
- 126. Gallaway M, Scheiman M, and Mitchell GL. Vision Therapy for Post-Concussion Vision Disorders. *Optom Vis Sci.* 2017;94(1):68-73.
- 127. Johns Hopkins Medicine. The Power of a Health Care Advocate. https://www.hopkinsmedicine.org/health/wellness-and-prevention/the-power-of-a-health-care-advocate. Accessed March 8, 2020.