

**LIMBIC-CENC Clinical Care Monograph Version 2**

**D. TBI, Medical Conditions, and Sensory Disorders**

from LIMBIC-CENC Knowledge Translation Center (LIMBICTM)

April 17, 2024, Richmond, VA

**D. TBI, Medical Conditions, and Sensory Disorders**

**Key Findings**

1. **TBI, Stroke, and Cardiovascular Disease**. LIMBIC-CENC researchers have identified that TBI is associated with an increased risk of all stroke. 1,2 Risk of stroke is highest in the first year post-TBI and remains elevated for 10+ years.1 There is a higher risk of hemorrhagic versus ischemic stroke after TBI.1 Veterans who sustained moderate-severe TBI are twice as likely to have a stroke than those with no TBI; Veterans who sustained mTBI are about 50% more likely to have stroke.1 Prevalence of cardiovascular disease is higher in Veterans with TBI compared to no TBI.2-5
2. **TBI and Epilepsy**. TBI is associated with an increased risk of epilepsy, is strongest in Veterans with moderate-severe TBI, and is present in Veterans with mTBI.5-7
3. **TBI and Pituitary Disorders**. LIMBIC-CENC research did not find mTBI to be a risk factor for pituitary disorders, i.e., growth hormone deficiency, hypothyroidism, or male hypogonadism.8
4. **TBI, Dizziness, and Balance**. LIMBIC-CENC researchers have identified that TBI increases the risk for dizziness, vestibular dysfunction, and balance impairments.9-12 The association between all three conditions was strongest in Veterans with moderate-severe TBI, but still present for mTBI.9, 11 As many as 40% of Veterans with post-mTBI dizziness may continue to have symptoms for years; predictors of poor dizziness prognosis include PTSD or hearing loss diagnoses, abnormal vestibular function, increased age, identification as a Black Veteran, and high school education level.11 Service Members and Veterans with 3+ mTBIs had a small but important decrease in balance performance on computerized posturography.12, 13 In addition to prior mTBI, pain has a strong relationship with poorer balance performance.12 Using diagnostic approaches that disrupt sensory inputs may help unmask balance deficits in Service Members and Veterans with mTBI.12, 14
5. **MTBI and Balance Phenotypes.** There is an interaction effect between number of mTBIs sustained and impairment of vision, vestibular or proprioception systems, that is associated with lower scores on dynamic posturography tests.15 In Service Members and Veterans with mTBI, 8 heterogeneous phenotypes of balance control with varying combinations of intact or impaired visual, vestibular and proprioception were identified.15 Overall findings indicated that all mTBI-related balance dysfunction does not cleanly fall under a vestibular dysfunction umbrella.15
6. **TBI and Hearing**. LIMBIC-CENC researchers have identified that TBI increases the risk of hearing loss and tinnitus and was strongest in Veterans with moderate-severe TBI and blast-related TBI.16, 17 Veterans with tinnitus diagnoses have higher rates of mental health diagnoses, including anxiety, depression, and substance use disorders, and higher annual health care utilization than those without tinnitus.18
7. **TBI, Cannabis Use Disorder (CUD), and Cognitive Disorders.** Progression to cognitive disorder was highest among those with a history of TBI and concomitant CUD followed by those with TBI only, and then CUD only compared to those without a TBI or CUD diagnosis.19

**Clinical Impact**

* **Policy to Increase Stroke Monitoring**. The associations between all severity-TBI and increased stroke risk are concerning and provide evidentiary support for policies to heighten monitoring of Veterans with a moderate-severe TBI history for traditional stroke risk factors. Future LIMBIC-CENC research using the PLS’ longitudinal follow-up data will identify subgroups of high risk mTBI Veterans who require early monitoring and intervention for stroke.
* **Epilepsy Treatment**. Except for penetrating TBI, routine prophylaxis with antiepileptic medication for epilepsy is not warranted after TBI of any severity.
* **Pituitary Disorder Screening**. LIMBIC-CENC research suggests that presence of mTBI should not be a risk consideration for hypogonadism, hypothyroidism, and growth hormone deficiency.
* **Increased Understanding of TBI and Balance Pathophysiology**. Our LIMBIC-CENC PLS research confirms that balance performance is a delicate and complex process controlled by brain networks that integrate and process multiple afferent and efferent pathways. Pain can also disturb pathways through a number of potential central or peripheral mechanisms. There is an apparent cumulative ‘dose effect’ of repetitive mild TBI on balance performance that may impact treatment requirements and lengthen the recovery course.
* **TBI and Balance Recommendations**. Our LIMBIC-CENC PLS findings suggest that use of balance diagnostics that disrupt sensory inputs, particularly vision, may lead to more efficient and effective diagnosis and treatment of balance disorders. Clinicians treating Service Members and Veterans with a TBI history should address pain before and during vestibular rehabilitation or other balance-related interventions. The further development and validation of TBI and balance phenotypes that include sensory impairments and pain will lead to vestibular rehabilitation protocols tailored to each individual's balance phenotype.
* **TBI and Hearing Loss Recommendations**. Our LIMBIC CENC findings on the frequent co-diagnosis of tinnitus, TBI, and hearing loss and increased risk of mental health disorders extend the current clinical research literature. These findings can improve the strength of evidence and recommendations for coordinated TBI, tinnitus/hearing loss, and mental health service care for Service Members and Veterans in future VA-DOD mTBI and hearing loss CPGs.
* **Brain Health and Wellness Tool**. LIMBIC-CENC findings on preventable behavioral health risk factors after TBI, synthesized with the current research literature, led to the development, testing, and release of the LIMBIC-CENC a brain health and wellness survey that generates personalized recommendations to support Service Members and Veterans efforts to identify and self-manage their health-related risk factors after TBI. The LIMBIC-CENC’s Brain Health and Wellness Video Series complements the survey tool and provides a series of 4-minute primers on how to identify, prevent or self-manage TBI and common symptoms that can impact function and quality of life.

**Primary Knowledge Translation Products**

* LIMBIC-CENC provides a repository of information on [TBI and Medical Conditions for SMs, Vs and Families](https://www.limbic-cenc.org/for-service-members-and-veterans-with-tbi/medical-conditions-veterans/) , [Sensory Function and TBI for Service Members, Veterans and Families](https://www.limbic-cenc.org/for-service-members-and-veterans-with-tbi/sensory-function-and-tbi-veterans/), [TBI and Medical Conditions for Clinicians](https://www.limbic-cenc.org/for-tbi-clinicians/medical-conditions-clinicians/) and [Sensory Function and TBI for Clinicians](https://www.limbic-cenc.org/for-tbi-clinicians/sensory-function-clinicians/).
* The [Abstract Veterans TBI Health and Outcomes Podcasts](https://www.limbic-cenc.org/for-service-members-and-veterans-with-tbi/the-abstract-veterans-tbi-health-and-outcomes-podcasts/) provide evidence-informed and real world patient, family and clinician perspectives on self-managing TBI and related health conditions.
* LIMBIC-CENC’s **Brain Health and Wellness Video Series** provides a 4 minute primer on how to identify, prevent or self-manage TBI and [Hearing Loss](https://www.youtube.com/watch?v=s4UVUlg_XcA&t=14s), [Hypertension](https://www.youtube.com/watch?v=eMe6GDOVNHk&t=3s), [Diabetes](https://www.youtube.com/watch?v=kPgH9Nv5BWA), and [Obesity, Activity, and Nutrition](https://www.youtube.com/watch?v=X596eBpKCiA).

**TBI and Co-occurring Medical Conditions References**

1. Schneider ALC, Peltz CB, Li Y, Bahorik A, Gardner RC, Yaffe K. Traumatic Brain Injury and Long-Term Risk of Stroke Among US Military Veterans. Stroke. 2023;54(8):2059-2068. doi: 10.1161/STROKEAHA.123.042360.. PMID: 37334708.
2. Stewart IJ, Amuan ME , Kennedy E, Kenney K, Werner JK, Carlson K, Tate D, Wright WS, Pogoda T, Dismuke C, Wilde E, Pugh MJ. Association between Traumatic Brain Injury and Subsequent Cardiovascular Disease Among Post-9/11 Veterans. JAMA Neurol 2022;79(11):1122-1129. doi: 10.1001/jamaneurol.2022.2682. PMID: 36066882.
3. Kornblith E, Bahorik A, Li Y, Peltz CB, Barnes DE, Yaffe K. Traumatic Brain Injury, Cardiovascular Disease, and Risk of Dementia among Older US Veterans. Brain Injury 2022;36(5);628-632.
4. Kennedy E, Panahi S, Stewart IJ, Tate DF, Wilde EA, Kenney K, Werner JK, Gill J, Diaz-Arrastia R, Amuan M, VanCott A, PughMJ. Traumatic brain injury and early onset dementia in Post 9-11 Veterans. Brain Inj. 2022 Apr 16;36(5):620-627. doi: 10.1080/02699052.2022.2033846. PMID: 35125061.
5. Byers AL, Li Y, Barnes DE, Boscardin WJ, Peltz CB, Yaffe K. TBI and risk of death in military veterans over 14 years: Injury severity, timing, and cause of death. J Psychiatr Res. 2022;156:200-205. doi: 10.1016/j.jpsychires.2022.09.035. PMID: 36257114.
6. Pugh MJ, Orman JA, Jaramillo CA, Salinsky MC, Eapen BC, Towne AR, Amuan ME, Roman G, McNamee SD, Kent TA, McMillan KK, Hamid H, Grafman JH: The prevalence of epilepsy and association with traumatic brain injury in veterans of the Afghanistan and Iraq wars. J Head Trauma Rehabil. 2015;30(1):29-37. doi: 10.1097/HTR.0000000000000045. PMID: 24695268
7. Pugh MJ, Kennedy E, Gugger J, et al: (2021). The Military Injuries-Understanding post-Traumatic Epilepsy Study: Understanding Relationships Among Lifetime TBI History, Epilepsy, and Quality of Life. J Neurotrauma 2021;38(20):2841-2850.
8. Walker WC, Werner JK, Agyemang AA, et al: Relationship of mild traumatic brain injury history to abnormalities on a preliminary neuroendocrine screen: a multicenter LIMBIC-CENC analysis. Brain Injury 2022;36(5):607-619.
9. Swan, A. A., Nelson, J. T., Pogoda, T. K., Akin, F. W., Riska, K. M., Hall, C. D., Amuan, M. E., Yaffe, K., & Pugh, M. J. (2020). Association of traumatic brain injury with vestibular dysfunction and dizziness in post-9/11 veterans. J/ Head Trauma Rehabil 2020;35(3). doi:10.1097/htr.0000000000000513
10. Swan AA, Akin FW, Amuan ME, Riska KM, Hall CD, Kalvesmaki A, Padilla S, Crowsey E,Pugh MJ: Disruptive Dizziness Among Post-9/11 Veterans With Deployment-Related Traumatic Brain Injury. *J Head Trauma Rehabil* 2022;37(4):199-212.
11. Akin FW, Swan AA, Kalvesmaki A, Hall CD, Riska KM, Stressman KD, Nguyen H, Amuan M, Pugh MJ. Factors That Impact the Long-Term Outcome of Postconcussive Dizziness Among Post-9/11 Veterans. Am J Audiol. 2023;32(3S):706-720. doi: 10.1044/2023\_AJA-22-00150. PMID: 37040302.
12. Walker WC, Nowak KJ, Kenney K, Franke LM, Eapen BC, Skop K, Levin H, Agyemang AA, Tate DF, Wilde EA, Hinds S, Nolen TL. Is balance performance reduced after Mild Traumatic Brain Injury?: Interim analysis from Chronic Effects of Neurotrauma Consortium (CENC) multi-centre study. Brain Inj 2018;32(10):1156-1168. doi: 10.1080/02699052.2018.1483529. PMID: 29894203.
13. van der Veen SM, Perera R, Fino PC, Franke LM, Agyemang AA, Skop K, Wilde EA, Sponheim SR, Stamenkovic A, Thomas JS, Walker WC. Sensory functions and their relation to balance metrics: a secondary analysis of the LIMBIC-CENC multicenter cohort. Front Neurol. 2023 Sep 14;14:1241545. doi: 10.3389/fneur.2023.1241545. PMID: 37780699; PMCID: PMC10538567.
14. van der Veen SM, Perera RA, Manning-Franke L, Agyemang AA, Skop K, Sponheim SR, Wilde EA, Stamenkovic A, Thomas JS, Walker WC. Executive function and relation to static balance metrics in chronic mild TBI: A LIMBIC-CENC secondary analysis. Front Neurol. 2023 Jan 11;13:906661. doi: 10.3389/fneur.2022.906661. PMID: 36712459; PMCID: PMC9874327.
15. Fino PC, Dibble LE, Wilde EA, Fino NF, Johnson P, Cortez MM, Hansen CR, van der Veen SM, Skop KM, Werner JK, Tate DF, Levin HS, Pugh MJV, Walker WC. Sensory Phenotypes for Balance Dysfunction After Mild Traumatic Brain Injury. Neurology. 2022;99(5):e521-e535. doi: 10.1212/WNL.0000000000200602. PMID: 35577572; PMCID: PMC9421603.
16. Swan AA, Nelson JT, Pogoda TK, Amuan ME, Akin FW, Pugh MJ: Sensory dysfunction and traumatic brain injury severity among deployed post-9/11 veterans: a chronic effects of neurotrauma consortium study. Brain Inj 2018;32(10):1197-1207. doi: 10.1080/02699052.2018.1495340. PMID: 30024786
17. Swan AA, Nelson JT, Swiger B, Jaramillo CA, Eapen BC, Packer M, Pugh MJ: Prevalence of hearing loss and tinnitus in Iraq and Afghanistan Veterans: A Chronic Effects of Neurotrauma Consortium study. Hear Res. 2017;349:4-12. doi: 10.1016/j.heares.2017.01.013. PMID: 28153668
18. Carlson KF, Gilbert TA, O'Neil ME, Zaugg TL, Manning CA, Kaelin C, Thielman EJ, Reavis KM, Henry JA: Health care utilization and mental health diagnoses among veterans with tinnitus. Amer J Audiol 2019;28(1S), 181-190.
19. Esmaeili A, Dismuke-Greer C, Pogoda TK, Amuan ME, Garcia C, Del Negro A, Myers M, Kennedy E, Cifu D, Pugh MJ. Cannabis use disorder contributes to cognitive dysfunction in Veterans with traumatic brain injury. Front Neurol. 2024 Jan 16;15:1261249. doi: 10.3389/fneur.2024.1261249. PMID: 38292293; PMCID: PMC10824930.

*LIMBIC-CENC research and its KT products were supported financially by the Department of Defense, Chronic Effects of Neurotrauma Consortium (CENC) Award W81XWH-13-2-0095 and Department of Veterans Affairs CENC Award I01 CX001135. Any opinions, findings, conclusions or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the views of the U.S. Government or the U.S. Department of Veterans Affairs, and no official endorsement should be inferred.*