

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

**C. MTBI, Mental Health, and Persistent Symptoms**

from LIMBIC-CENC Knowledge Translation Center (LIMBICTM)

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**Key Findings**

1. **MTBI and PTSD**. About 40% of Service Members and Veterans with mTBI screened positive for PTSD compared to about 25% without mTBI.1  Service Members and Veterans with both mTBI and PTSD have the highest rates of depression symptoms, pain, and sleep apnea risk relative to those without either condition.2 Service Members and Veterans with PTSD, irrespective of mTBI history, had high rates of obesity, sleep problems, depression, and pain.2 For Veterans with both TBI and PTSD who receive cognitive processing therapy for trauma, worse baseline sleep quality was associated with less improvement in PTSD and cognitive symptoms.3
2. **MTBI and Persistent Symptoms**. Service Members and Veterans with mTBI report more neurobehavioral symptoms compared to those without mTBI.1 A dose-response association was found between greater number of mTBIs (blast-related or non-blast) and increased rates and severity of self-reported neurobehavioral symptoms and pain among Service Members and Veterans.4-6 An association was also identified between PTSD symptom severity, low social support, deployment-related mild TBI, and increased risk of behavioral dyscontrol.7
3. **Neurobehavioral Symptom Inventory (NSI)**. The NSI has four symptom clusters (somatosensory, affective, cognitive, and vestibular) that have been validated in the LIMBIC-CENC PLS cohort with factor analytic techniques.1 NSI clusters show evidence of good reliability and validity.1
4. **MTBI and Cognitive Performance**. LIMBIC-CENC research did not find evidence that presence or number of mTBIs directly impacted cognitive performance including attention, working memory, executive function, and processing speed.7, 8 Sleep disorders, PTSD, and pain decreased cognitive performance.9 Evidence suggests that telehealth delivery of group cognitive rehabilitation and aerobic activity are promising interventions to improve cognition following mTBI.10, 11
5. **MTBI and Sleep Disorders**. Veterans with a mTBI history were about 40% more likely to develop a sleep disorder of any type including sleep apnea, insomnia, hypersomnia, and sleep-related movement disorders.12 The association with mTBI remained consistent over time; PTSD had little effect.12 Obstructive sleep apnea has a stronger relationship to neurocognitive function than mTBI history.9 Poor sleep is associated with sequelae of TBI including executive dysfunction and with exosomal microRNA differences previously implicated in psychiatric disorders, progressive neurodegeneration, and vascular physiology.13
6. **MTBI and Depression.** Service Members andVeterans depression symptoms were greater for those with a history of multiple mTBIs compared with those who had a single mTBI or no TBI.14 Service Members andVeterans depression symptoms were greater for those who had a single mTBI compared to no TBI.14 Combat deployment-related injuries were associated with higher depression scores than injuries occurring in non-combat or civilian settings.14 Service Members and Veterans increased rates of depression after mTBI persisted in the absence of PTSD.14

**Clinical Impact**

* **Inclusion of Service Member and Veteran Issues in Revised mTBI Case Definition.** LIMBIC-CENC findings and research leadership played a critical role in the consideration and incorporation of Service Member and Veteran-centric issues into the 2023 Revised ACRM mTBI Case Definition.15
* **Policy Recommendations for Holistic Approaches to mTBI Treatment**. LIMBIC-CENC findings have helped differentiate the effects of co-occurring mTBI, PTSD, depression, pain, behavioral dyscontrol, and sleep disturbance. These findings extend the current literature and strengthen evidence for DOD and VHA healthcare policies that emphasize: (1) early, comprehensive, assessment and personalized, (2) holistic treatment to manage symptoms and reduce chronicity, and (3) improved social support systems. When treating Service Members and Veterans with a history of mTBI and chronic cognitive performance issues, employing a holistic approach is important to assess and treat the most common causes, i.e., sleep disorders, PTSD and pain.
* **Recommendations for Early Sleep Assessment and Treatment**. Growing and converging biological (serum markers, neuroimaging) and epidemiological (prognostic) findings from LIMBIC-CENC researchers point to sleep disturbance as a potential primary root cause for Service Members and Veterans cascading post-mTBI symptoms and neurodegeneration risk. Early identification, treatment, and prevention strategies for post-TBI sleep disorders are critical but understanding the evolution of post-TBI sleep disturbance and its impact on other symptoms remains elusive. LIMBIC-CENC research protocol development is underway to identify real-time, longitudinal digital biomarkers of early sleep, depression, acute stress, and pain to better inform post-mTBI symptom evolution, prognosis, and treatment targets.
* **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 co-morbid risk factors that can decrease impact of co-morbid and secondary conditions.
* **Need for Personalized mTBI and Mental Health Treatment**. LIMBIC-CENC research is underway to further develop mTBI mental health phenotypes that identify subgroups of Service Members and Veterans with common symptoms, biomarkers and root causation in order to tailor personalized treatment algorithms for each sub-phenotype.
* **Policy Recommendations on the Need for Secondary TBI Prevention Strategies**. Our findings on the linear associations between number of mTBIs and increased symptom frequency, severity and chronicity make clear that DOD-VA policy recommendations must prioritize proactive, secondary TBI prevention strategies.

**Primary Knowledge Translation Products**

* LIMBIC-CENC provides a repository of information on [Mental Health and TBI for SMs, Vs and Families](file:///\\rams.adp.vcu.edu\SOM\Shares\PMR\LIMBIC-CENC\Knowledge%20Translation\Clinician%20KT%20Products\Monographs\Mental%20Health%20and%20TBI%20for%20SMs,%20Vs%20and%20Families), [TBI and Wellness for Service Members, Veterans, and Families](https://www.limbic-cenc.org/for-service-members-and-veterans-with-tbi/wellness-veterans/), [Mental Health and TBI for Clinicians](https://www.limbic-cenc.org/for-tbi-clinicians/mental-health-clinicians/), and [TBI and Wellness for Clinicians](https://www.limbic-cenc.org/for-tbi-clinicians/wellness-clinicians/).
* LIMBIC-CENC’s **Brain Health and Wellness Video Series** provides 4-minute, easy to read and apply primers on how to identify, self-manage or prevent [TBI and Depression](file:///\\rams.adp.vcu.edu\SOM\Shares\PMR\LIMBIC-CENC\Knowledge%20Translation\Clinician%20KT%20Products\Monographs\TBI%20and%20Depression), [TBI and PTSD](file:///\\rams.adp.vcu.edu\SOM\Shares\PMR\LIMBIC-CENC\Knowledge%20Translation\Clinician%20KT%20Products\Monographs\TBI%20and%20PTSD), [TBI and Tobacco Use](https://www.youtube.com/watch?v=SJ6Vawx4qkU), [TBI and Alcohol Use](https://www.youtube.com/watch?v=3D5y_lsjTJc&t=49s), and [TBI and Sleep](https://www.youtube.com/watch?v=ODlHArfPSJo). The series also provides links to self-management tools and/or access to healthcare services for mental health and chronic symptoms.
* 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 assessing and self-managing TBI, mental health conditions, and symptoms.

**MTBI, Mental Health and Persistent Symptom References**

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