

Sound Sleep, a Crucial Component of Military Medicine's Armamentarium?

Commentary on Macera et al. Do sleep problems mediate the relationship between traumatic brain injury and development of mental health symptoms after deployment? *SLEEP* 2013;36:83-90.

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It is 2007 and three Marines in the lead vehicle of a platoon convoy traveling through east-central Iraq encounter a remotely detonated roadside improvised explosive device (IED). The blast demolishes the front of vehicle as it comes to a violent halt in the IED-excavated crater. The Marines experience traumatic brain injury (TBI) via strong acceleration-deceleration forces and shear stresses on various brain structures as well as a high-pressure blast wave. All three lose consciousness but survive.

The Marines are recovered to their forward operating base, undergo several days of evaluation, treatment, and observation, but soon resume field operations. During their remaining deployment, one of the Marines experiences worsening of previously troubled sleep patterns, and another has new-onset of severe insomnia.

Following deployment, the Marines return to their US base. During demobilization, they are assessed by questionnaire about exposure to TBI and sleep and mental health problems. Over the ensuing months, they reintegrate into their US-based lives and experience a variety of typical wartime family-, financial-, and health-related stresses. Some months later, they are reassessed and report new or worsening mental health symptoms.

The preceding account is fictionalized but based on real events and is unfortunately representative of myriad similar scenarios experienced by service members who participated in Operation Iraqi Freedom and the ongoing Operation Enduring Freedom. We would like to be able to make sense of this too-common scenario to better understand whether proactive interventions—rather than the reactive treatment of downstream mental health manifestations—might arrest the development of service-related mental health problems. Can TBI experienced during deployment cause sleep pathology? Can this sleep pathology cause or amplify mental health outcomes? And, can the “signal” of causal associations between TBI, sleep, and mental health be separated from the “noise” of many other factors affecting service members' health? If the answer to these questions is “yes,” then there may be hope that the process by which TBI evokes common service-related mental health pathologies such as depression and posttrau-

matic stress disorder (PTSD) might be interrupted by preventing or treating sleep problems.

Indeed, there is evidence that: (1) TBI increases risk of depression and PTSD^{1,2}; (2) TBI is associated with disturbed sleep, sleepiness, and polysomnographic EEG abnormalities³⁻⁶; and (3) sleep pathologies predict development of depression and PTSD.⁷⁻¹¹ Thus, the potential for sleep disturbance to serve as an intermediary on a pathway from TBI to mental health pathology is supported.

In this issue of *SLEEP*, Macera and colleagues¹² attempt to measure the degree to which sleep problems mediate an association of TBI and development of depression or PTSD. They do so with a longitudinal examination of male Navy and Marine Corp service members who participated in Operations Iraqi Freedom or Enduring Freedom and returned from deployments in 2008-2009. The approximately 29,000 service members in the sample were predominantly enlisted active duty Marines. At the end of deployment, the Marines and Sailors answered questionnaires that included items assessing exposure to TBI (deployment-related head injury resulting in lost consciousness; feeling dazed or confused; seeing stars; and/or an inability to remember the injurious event), depression and PTSD symptomatology, and a question about “problems sleeping or still feeling tired after sleeping.” A similar follow-up questionnaire was administered from one to several months later. The authors then employed a commonly used statistical technique to examine evidence of a mediation process associating TBI with sleep problems and then sleep problems with subsequent development of depression or PTSD in the months post-deployment.

The investigators estimated that—after accounting for service members' pay grade, age, combat experiences, and other factors—26% percent of the association of deployment-related TBI with new-onset post-deployment PTSD may be mediated by sleep problems occurring prior to PTSD. Similarly, sleep problems were found to mediate 41% of the association between TBI and depressive symptoms. These figures do not have a straightforward biological or clinical interpretation (e.g., one cannot infer that 41% of TBI-caused depression would be prevented by treating sleep problems). Nevertheless, the findings justify hypothesizing that efforts to treat sleep problems in service members recently experiencing TBI may reduce the risk of downstream depression and PTSD.

While the study of Macera et al.¹² yielded an important finding, the usual methodologic difficulties facing observational research apply and may conspire to diminish or exaggerate measured associations. Classification of key variables was not based on comprehensive clinical assessments, but on a brief set

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of questionnaire items. “Sleep problems” were assessed non-specifically. Depression, PTSD, and TBI symptoms can overlap and are highly subjective. Service members may be motivated for a variety of reasons to underreport such symptoms,¹³ especially immediately post-deployment when self-reporting of mental health symptoms may lead to a delay in authorization to take leave (or delayed release from active duty for reservists). Imperfect questionnaire sensitivity and specificity often mask true causal associations. However, if some service members tended to be more or less willing to disclose clusters of symptoms at one time point, or over time, this could result in spuriously elevated correlations between the symptoms. Additionally, accurate estimation of mediation parameters requires measuring unconfounded pairwise associations between TBI, sleep problems, and depression (or PTSD). This can be difficult since, for example, factors such as ongoing family-related stress or non-TBI injuries that underlie both persistent insomnia symptoms and risk for developing depression can bias mediation parameter estimates even if those factors are unrelated to TBI (e.g., via a “collider bias”).¹⁴

Despite these methodologic challenges, we believe the findings of Macera and colleagues¹² and prior literature are compatible with a link between TBI and elevated risk of depression and PTSD, partially mediated by sleep problems. These findings have continuing relevance since service members participating in Operation Enduring Freedom remain exposed to a high burden of TBI—an injury that has been increasingly prominent in the last decade as advances in battlefield protective gear and medicine have allowed service members to survive injuries that would have been fatal in previous eras. We therefore have three recommendations. First, we recommend thorough and repeated screening for sleep problems in post-deployment service members. Second, there is a need for research to further extend the findings of Macera and colleagues, ideally with highly sensitive and specific approaches for identifying key variables. In addition to standard screening practices, supplemental anonymous screening of service members’ depression and PTSD symptoms would likely increase symptom-reporting and enhance future research efforts in this area.¹³ Thirdly, effective treatments of sleep problems, *appropriate to the circumstances of deployed and recent post-deployment service members*, should be investigated. There is a substantial knowledge gap in effective treatment of sleep disturbances in TBI, and there is some concern that commonly used pharmacological agents for insomnia may adversely affect neuroplasticity.¹⁵ Appropriate treatment will likely include a significant nonpharmacological component, such as tailored cognitive behavioral therapy.¹⁶ We applaud Macera and coauthors for their important analysis and expect that it will serve as an impetus for further study and ultimately result in better health for our service members.

CITATION

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