Pathophysiology of Neurotrauma

New Insights into Mechanisms of Mild Traumatic Brain Injury

Explosive blasts produce one of the most common types of traumatic brain injury (TBI) associated with the military, and increased use of improvised explosive devices in combat zones warrants the study of direct effects blast shockwaves have on the brain. Researchers at John Hopkins University (JHU) developed a mathematical model of brain cortical activity developed that has led to new insights about brain dynamics, which will facilitate diagnosis and treatment of blast-induced mild traumatic brain injury (mTBI) in Service members (*Boothe et al. 2017*; Figure 1). Working in concert with JHU researchers, Army Research Laboratory scientists have for the first time established how the large-scale deficiencies in sensory processing that are found in mTBI cases can result from neuronal damage at the cellular level, and could be observed as a reduction in power in the 1 to 40 hertz frequency range local field potential (*Boothe et al. 2017*). This new understanding of multiscale brain dynamics is particularly needed in cases of mTBI in which morphological changes that are detectable through commonly-used diagnostic techniques, such as magnetic resonance imaging, are not present. Next steps involve creating a model that represents specific areas of the cortex to more accurately determine how mTBI and other injuries affect Service member performance.

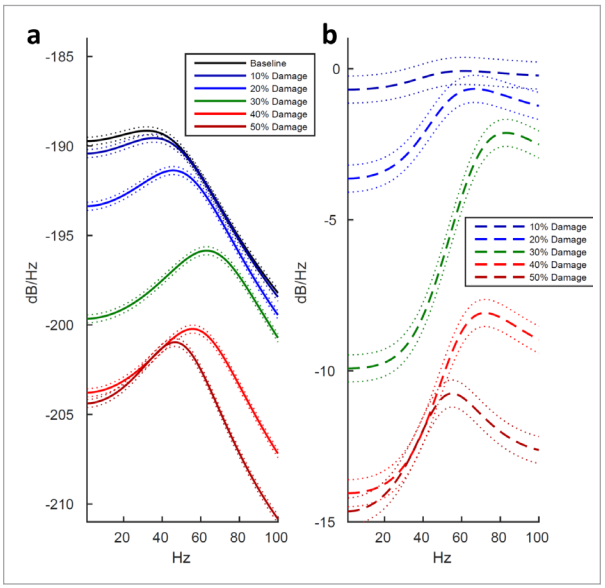

FIGURE 1: Effects of cell membrane damage on spectral power of simulated local field potential. Across both plots, colored lines represent different levels of damage to the cell membrane (black is baseline and damage increases from blue to red in increments of 10 percent), and dotted lines indicate 99 percent CIs. (A) Effect of damage to the whole cell. (B) Difference in log-scaled spectral power between baseline (undamaged) and simulated damage to the whole cell. As expected, power is reduced at higher levels of simulated damage, but all frequencies are not affected equally. In the lower frequencies, ranging from 1 to 40 hertz, there is drop in power of approximately 14 decibels per hertz between the 10 and 50 percent levels of damage. Likewise, in the 40–100 hertz range power drops 12 decibel per hertz. (Figure 3 from Boothe et al. (2017) used with permission from the authors)

Results from this study indicate that detonated Research Department eXplosives, also known as T4 explosives cause distinct losses of synaptic proteins before cell death, perhaps explaining the cognitive deficits in those blast-induced TBIs with no detectable neuropathology. Researchers at Walter Reed Army Institute of Research (WRAIR) are examining this research to see if it can supplement their ability to identify molecular markers of blast-induced injury to neurons in sensitive brain areas to enable the eventual production of a field-ready biomedical device capable of identifying traumatic brain injury (TBI) in Service members. Outcomes from this study have the

potential to transition to WRAIR preclinical brain injury neuroprotection research to initiate drug interventions in moderate and severe TBI patients.

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REFERENCES:

Boothe, D. L., Yu, A. B., Kudela, P., Anderson, W. S., Vettel, J. M., and Franaszczuk, P. J. 2017. "Impact of Neuronal Membrane Damage on the Local Field Potential in a Large-Scale Simulation of Cerebral Cortex." Front Neurol 8:236. doi: 10.3389/fneur.2017.00236.