Public Abstract

Focus Area: Mitigation and treatment of traumatic injuries, war-related injuries, and diseases to ocular structures and the visual system.

Rationale: Ocular trauma occurs in 13% of the injuries sustained by wounded soldiers in active combat zones, with damage to the retina occurring in at least 50% of these same eye injuries. Primary blast-induced injury (PBI), which can occur in eyes that are not punctured or ruptured by the blast, is correlated with a high degree of permanent visual impairment. The cause of this deterioration of visual function is currently unknown. However, one aspect of injury that is thought to contribute to permanent visual loss is the combination of chronic ischemia and resulting neurotoxicity that greatly affect function of the retina. In retinas where these processes occur, their effects ultimately can lead to irreversible neurodegeneration of the delicate, light-sensing photoreceptor neurons, which are essential to proper visual function.

Retinal ischemia is caused by insufficient oxygen levels reaching the retinal neurons. Neurons such as the photoreceptors alter their cellular behavior under these hypoxic stress conditions and eventually begin to die if oxygen levels are not restored to normal. One possible cause of ischemia/hypoxia in the retina is damage to the choroidal vasculature that supplies oxygen to the retina. The choroidal capillaries that supply the retina can become damaged following PBI injury, leading to oxygen starvation of the photoreceptors. Altered cellular behavior may be driven by TRPM7, which is present in photoreceptor neurons. TRPM7 function is influenced by cellular oxygen supplies and may regulate hypoxia-induced cellular stress responses in photoreceptors themselves.

Objective: Our aim is to examine the potential link between trauma-induced hypoxic/ischemic conditions in the choroid and anoxic activation of TRPM7 leading to photoreceptor cell death. Using the mobile biophotonics device developed in this proposal to measure blood oxygen levels in the eye following an injury and the function of TRPM7 in regions of the retina underlying damaged choroidal blood vessels, we seek to understand how long-term, permanent vision loss results from traumatic eye injuries.

Applicability and Potential Impact: The described research seeks to stabilize and improve long-term vision in combat veterans who have sustained primary blast injuries (PBI) to the eye without physical rupture or puncture of the eye. Retinal injury results in over 50% of sustained combat eye injuries and likely contributes to long-term vision loss after the initial injury. By understanding the role TRPM7 plays in hypoxic stress, it may be possible to halt vision loss by inhibiting abnormal TRPM7 function, thus aiming to return its function to normal, or by developing oxygen-based therapies to mitigate the initial progression of hypoxia.

Military Benefit: Our research seeks to provide a mobile endoscope probe with the potential to be used by military clinicians to quickly evaluate traumatic eye trauma on the spot. In addition to validating this application, our work with TRPM7 seeks to clarify the role of...
oxygen, Ca2+, and Mg2+ in traumatic injuries. The long-term goal of this research is to develop treatments for PBI and hypoxia by controlling these chemical insults in affected tissue.