Therapies for TBI-related Symptoms

Epigenetic Rescue of Injury Circuits in Brain Following Blast-induced TBI

Researchers at the USUHS Department of Anatomy, Physiology, and Genetics, sponsored by the Henry M. Jackson Foundation for Military Medicine, are investigating epigenetic changes induced by blast exposure. The researchers specifically studied whether epigenetic-regulated proinflammatory processes regulate the sensitivity of the amygdala and other parts of the frontolimbic circuit in the blast-exposed brain. Rats were subjected to blast injury and the following effects were measured: (1) epigenetic changes in the amygdala 24 hours after blast; (2) changes in the levels of a proinflammatory DNA-binding protein in activated immune cells in the amygdala; and (3) the ability of the histone deacetylase (HDAC) inhibitor suberanilohydroxamic acid (SAHA; also known as Vorinostat and marketed as Zolinza®) to reverse the clinical and molecular effects of blast exposure. Levels of HDAC two, four, and six significantly increased 24 hours after blast exposure. In the amygdala, levels of [pSer337]NFκB-p1-5/p50 and [pSER32/36]IκBα, both pro-inflammatory DNA binding proteins, significantly increased. Finally, SAHA treatment blocked HDAC activities in the brain, and pretreatment with SAHA reversed blast-induced sensory deficits 24 hours after blast. These findings support the possibility of using a safe, FDA-approved drug from the class of HDAC inhibitors to rescue cognitive impairment following blast exposure.