Staying Ahead of the Hit: Using Drosophila melanogaster as an Integrated Model to Elucidate the Neuropathology, Physiology, and Genetic Mechanisms Underlying Traumatic Brain Injury

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Background: Traumatic brain injury (TBI) is a leading international cause of morbidity and mortality. The neurologic outcome of TBI is significantly influenced by the cellular, molecular and physiologic responses (secondary injury), to the initial impact, which are poorly understood. The goals of this project were to: 1) To assess the level of apoptosis in brains of Drosophila subjected to TBI, 2) To characterize the role of the immune system after TBI, by quantifying the level of expression of 2 anti-microbial peptides (AMP) genes (Attacin C and Diptericin B), and 3) To observe the effect TBI has on the sleep-wake patterns of flies. Methods: A “high-impact trauma” (HIT) device was built, which used a spring-based mechanism to propel flies against the wall of a vial, causing mechanical damage to the brain. Immune response was assessed using mRNA from the heads of flies and qRT-PCR of 2 Anti-Microbial Peptides (AMPs). An antibody to cleaved-Caspase-3 was used as a general apoptotic marker in Drosophila brains. Circadian behavior was assessed using a locomotor assay and the Drosophila Activity Monitor system. Results: TBI flies showed an enhanced innate immune response shown by increased gene expression of the anti-microbial peptides. Increased apoptosis was detected in TBI brains, by measuring cleaved caspase activity. More flies with TBI demonstrated altered sleep and circadian rhythms with males and females having distinct differences. Conclusion: TBI causes distinct biochemical and genetic alterations and an improved understanding of these secondary sub-cellular mechanisms of TBI is a vital prerequisite to developing effective interventions.

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