A Machine Learning-Based Approach for Characterization of Neurological Proteomic Biomarkers in a Mouse TBI Preclinical Model

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News reports of car injuries and sports concussions have shed light on a new "silent pandemic" for the current era: Traumatic Brain Injury (TBI). TBI induces a cascade pathway within neural cells, leading to apoptotic and necrotic death, in which astroglia and neurons lyse and release protein biomarkers. The present study utilized a transgenic human Tau mouse model to relate brain injury after controlled cortical impact (CCI) to changes in prospective biomarker concentrations over time, for improved diagnosis of TBI with respect to severity and locality. Tissue and serum samples were extracted from genotyped human Tau mice. Samples were tested using ELISA to determine concentration of biomarker in naive and CCI-injured mice. Tissue data showed that pTau served as a primary biomarker for acute cortical injury after severe TBI (unpaired t-test, t-2.827, $p = 0.0368$). GFAP served as a biomarker for both acute and chronic hippocampal injury (unpaired t-test, t-9.959, $p<0.0001$; unpaired t-test, t-7.989, $p<0.0001$). Serum samples displayed that GFAP and pTau were acute and chronic biomarkers of severe TBI, while NFL and UCH-L1 were acute biomarkers. Tissue results provided greater evidence of localization and post-mortem utility, while serum data had clinical utility. A random forest algorithm was developed to assess the validity of utilizing a multivariate panel of biomarkers in detection of TBI, relating several parameters from immunohistochemistry staining and ELISA to TBI diagnosis. The RF model provided evidence for hyperacute panel testing and the relative strength of serum samples, the first of its kind to do so. These findings suggest that objective blood/tissue tests can detect TBI and effectively overcome the price and lack of specificity associated with neuroimaging,