Decoding the Underlying Neural Activity of Neurodegeneration in Traumatic Brain Injury

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Traumatic brain injury (TBI) is a prevalent form of acquired injury that can lead to permanent disabilities and increased mortality. 90% of all TBI patients suffer visual impairment resulting from damaged retinal ganglion cells (RGCs), and, despite its far-reaching implications, few successful treatments have been implemented. Notably, activity-induced neuroprotection based on sound and light stimuli is shown to be possible. We hypothesized that the modulation of neural activity could protect RGCs following TBI. Bulk RNA-seq data from activity-modulating treatment were obtained, and bioinformatics analyses were performed. Activity-induced neuroprotection was found to be strongly associated with the downregulation of synaptic calcium signaling and cholinergic transmission. Candidate genes were screened in consultation with the Allen Brain Atlas Transcriptomics Explorer. Unlike previous reports indicating that positive modulators of the alpha-7 nicotinic cholinergic receptor (nAChR) rescued memory impairments post-injury, in vivo CRISPR-mediated knockouts of neural activity-modulating gene Chrnb4 – nAChR beta-4 subunit – and its downstream gene Plcb4 were found to protect RGCs to varying degrees. Our results implicate that distinct nAChR subtypes may influence activity-regulated neuronal survival differently. Our study suggests that certain auditory stimuli, potentially music, could be designed for TBI patients, which would aid treatment by modulating neural activity. Additionally, we demonstrated that nAChRs are potential therapeutic targets for novel neuroprotective drug discovery and delivery, which, in turn, will benefit patients clinically.

Awards Won:

Second Award of $2,000