Aged astrocytes maladaptively contribute to the neuroinflammatory milieu following TBI

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Abstracts will be considered for both poster and platform presentations

Neurotrauma (TBI, spinal cord injury, etc.)

Advanced aging is one of the most powerful predictors for the incidence and vulnerability to a traumatic brain injury (TBI). Problematically, aged survivors of TBI are almost 40% more likely to develop progressive neurodegenerative disorders compared to young. Moreover, aged survivors of TBI exhibit significant impairments in functional recovery as well as increased comorbidities following TBI. Despite the increased risk and poorer outcomes, strikingly little is known about how TBI differentially affects the brain in the aged, compared to young. Classically, the current dogma regarding neuroinflammatory research following TBI has focused on the primary innate immune effector (e.g. microglia) of the brain. However, it is becoming increasingly apparent that astrocytes participate in the neuroinflammatory response of during disease, yet there is a current gap in research knowledge aimed at understanding how these cells respond to TBI. In the current study, we examined how and when aged astrocytes differ from young astrocytes following TBI across acute and subacute post-injury intervals. TBI was reproduced using the focal controlled cortical impact method on young (3m) and aged (18m) C57BL6 mice. We examined three post-injury intervals; 1, 3, and 7 days. Using these intervals, we generate two cohorts of mice, one for histology and the second for gene expression assays. To examine astrocyte-specific responses we validated a novel method for enriching astrocytes from the injured parenchyma to use for gene expression profiling. RNA from enriched astrocytes was analyzed using gene arrays to model the multivariate inflammatory response as a function of age and post-injury interval. Histologically, our data demonstrate that astrocyte reactivity peaks at 3d interval in young, however, in the aged mice this response progressively increases through 7d post-injury. Gene expression was assessed by two complimentary methods; TaqCard and NanoString. Genes examined using the TaqCard array represent putative astrocyte-specific genes previously identified by RNAseq studies, while the NanoString array quantifies a variety of genes specific to inflammatory response. Our novel findings indicate that following TBI, aged astrocytes have a disproportionate and protracted response for multiple genes previously identified as ‘ischemic-induced’, compared to young. Moreover, our NanoString arrays showed significantly elevated expression of multiple chemokines, cytokines, and inflammatory transcriptional factors in aged astrocytes, compared to young. Collectively, our data identify several novel gene candidates that are uniquely responsive or exacerbated in the aged astrocytes condition following TBI. Therefore, ongoing work to examine if manipulating these aged responses may represent future therapeutic targets to prevent the aberrant response to TBI in aged individuals.