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Microglial process convergence on acutely injured axons following diffuse traumatic brain injury

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Mild traumatic brain injury (mTBI) is a highly prevalent disease with devastating costs. While one of the major pathological hallmarks of TBI is diffuse axonal injury (DAI), neuroinflammation occurring chronically, weeks to months following injury, has also been implicated in a variety of detrimental as well as regenerative functions. Currently, little is known regarding acute neuroinflammation occurring within the first day following mTBI, particularly within the gyrencephalic brain. Therefore, we assessed acute neuroinflammation at 6h and 1d in a unique model of diffuse mTBI in the micro pig. Mild TBI did not precipitate systemic physiological abnormalities or overt histopathological damage; however, this micropig model generated substantial DAI in the thalamus, an area commonly affected in human mTBI, at both 6h and 1d following injury. Extensive acute neuroinflammation was also observed following mTBI within the thalamic domain. Importantly, the processes of activated microglia converged on axons sustaining DAI at both time points following mTBI. Contacts between activated microglia processes and swellings of injured axons increased two fold at 6h and nearly fourfold at 1d following mTBI compared to associations with uninjured myelinated axons in sham animals. While active phagocytosis was observed in association with wallerian degeneration following mTBI, the microglia that contacted swellings from diffusely injured axons were not ultra-structurally phagocytic. This study shows direct physical correlation between injured axonal swellings and non-phagocytic acute neuroinflammation in a higher order animal, finding that could lead to novel diagnostics based on a more complete understanding of acute neuroinflammation following mTBI.

Recent Publications

1. A D Lafrenaye, M Todani, S A Walker, J T Povlishock (2015) Microglia processes associate with diffusely injured axons following mild traumatic brain injury in the micro pig. Journal of Neuroinflammation 12: 186.
2. A D Lafrenaye (2016) Physical interactions between activated microglia and injured axons: Do all contacts lead to phagocytosis? Neural regeneration research 11:538-40.

Biography

Audrey D Lafrenaye is a Research Associate Faculty Member in the Department of Anatomy and Neurobiology at Virginia Commonwealth University. She has received her PhD in Anatomy. Following her graduate work she transitioned into the trauma field. Her research focuses on evaluating the diffuse pathologies following traumatic brain injury. In the conduct of her studies she utilizes both rodent and micro pig models of diffuse traumatic brain injury and has been particularly interested in the effects of elevated intracranial pressure without hypoperfusion on sub-acute pathology and morbidity following TBI. For the past few years she has explored the pathological progression of diffuse axonal injury and acute neuro-inflammation following mild diffuse traumatic brain injury in the pig.

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