Traumatic Brain Injury Leads to Development of Parkinson's Disease in Mice

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TBI is an insult to the brain from the application of external physical force that leads to temporary or permanent structural and functional impairment of the brain. The long-term consequences of TBI are closely associated with the development of histopathological deficits. It has long been suggested that prior TBI increases the subsequent incidence of chronic neurodegenerative disorders, including Parkinson disease (PD), which is characterized by a gradual degeneration of the nigrostriatal dopaminergic neurons. However, preclinical studies on the pathophysiological changes in substantia nigra (SN) after chronic TBI are lacking. In the present in vivo study, we examined the pathological link between PD-associated dopaminergic neuronal loss and chronic TBI. Thirty days post-TBI (corresponding to 5-6 years in human), rats were euthanized and brain tissues harvested. Immunostaining was performed using tyrosine hydroxylase (TH), an enzyme required for the synthesis of dopamine in neurons, α-synuclein, a presynaptic protein that plays a role in synaptic vesicle recycling, and inflammatory glia cells markers, all key players in PD pathology. Specifically, TBI was induced in mice by controlled cortical impactor. At different time points behavioral tests (Open field, Elevated plus maze tests and Barnes maze) were performed. Our results revealed a significant decrease of TH-positive expression in the surviving dopaminergic neurons of the SN pars compacta (SNpc) relative to sham control, such as dopamine transporter (DAT), and a significant behavioral alterations. In addition, a strong increase in neuroinflammation evaluated as GFAP, TNF-α, COX-2, iNOS expressions, IκB-α degradation, and NF-κB translocation, was evident. Also, neurotrophic factors expression such as BDNF, NT3, NGF, GDNF was also decreased at 30 days after TBI. Interestingly, our results showed increased α-synuclein accumulation in microglia compared to astrocytes.
In conclusion, we suggested that there are currently under-appreciated biological mechanisms linking brain injury and neurodegenerative diseases.