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Cellular Senescence and Neuroinflammation Following Controlled Cortical Impact Traumatic Brain Injury in Juvenile Mice

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Abstract : Traumatic brain injury (TBI) is the leading cause of disability and death in young adults and also increases the risk ofneurodegeneration. The mechanisms linking moderate to severe TBI to neurodegeneration are not known. It has been proposed that cellular senescence inductionpost-injury could amplify neuroinflammation and induce long-term changes. The impact of these processes after injury to an immature brain has not been characterised yet. We carried out a controlled cortical impact injury (CCI) in juvenile 1 month-old male CD1 mice. Animals were anesthetised and received a unilateral CCI injury. The sham group received anaesthesia and had a craniotomy. A naïve group had no intervention. The brain tissue was analysed at 5 days and 35 days post-injury using immunohistochemistry and markers for microglia, astrocytes, and senescence. Compared tonaïve animals, injured mice showed an increased microglial and astrocytic reaction early post-injury, as reflected in Iba1 and GFAP markers, respectively; the GFAP increase persisted in the later phase. The senescence analysis showed a significant increase inγH2AX-53BP1 nuclear foci, 8-oxoguanine, p19ARF, p16INK4a, and p53 expression in naïve vs. sham groups and naïve vs. CCI groups, at 5 dpi. At 35 days, the difference was no longer statistically significant in all markers. The injury induced a decrease p21 expression vs. the naïve group, at 35 dpi. These results indicate the induction of a complex senescence response after immature brain injury. Some changes occur early and may reflect the activation/proliferation of non-neuronal cells post-injury that had been hindered, whereas changes such as p21 downregulation may reflect a delayed response and pro-repair processes.
Keywords : cellular senescence, traumatic brain injury, brain injury, controlled cortical impact
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