FORMYL PEPTIDE RECEPTOR 1SIGNALLING IN ACUTE INFLAMMATION AND NEURAL DIFFERENTIATION INDUCED BY TRAUMETIC BRAIN INJURY

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Introduction: Traumatic brain injury (TBI) is a shocking disease frequently followed by behavioural disabilities including risk of cerebral atrophy and dementia. N-formylpeptide receptor 1(FPR1) is expressed cells and neurons in the central nervous system. It is involved in inflammatory processes and during the differentiation process in the neural stem cells.
Materials and Methods: We investigate the effect of the absence of Fpr1gene expression in mice subjected to traumatic brain injury from the early stage of acute inflammation to neurogenesis and systematic behavioral testing 4weeks after injury.

Results: TBI Fpr1KO mice showed reduced histological impairment, tissue damage and acute inflammation. Twenty-four hours after injury molecular analyses indicated that in absence of Fpr1there was reduced NF-κB signalling induction, NRLP3inflammasome pathway activation and oxidative stress increase. Conversely, four weeks after TBI immunohistochemical analyses indicated increased surviving proliferated cells in the Dentate Gyrus of WT group while TBI Fpr1KO mice did not show any significant neurogenesis. Behavioral analysis confirmed this trend: Novel Object Recognition test and Morris water maze test showed the compromised cognitive function of TBI Fpr1KO group; Social Behavior Test showed TBI Fpr1KO mice reduced reciprocal social interaction; Open Field test showed TBI Fpr1KO mice locomotor deficit. Four weeks after TBI molecules associated with neuronal differentiation were assessed: in absence of the Fpr1gene expression animals subjected to TBI displayed reduced neural differentiation while up-regulation of astrocytes differentiation.

Discussion: The activation of the Fpr1increased inflammation and oxidative stress immediately after traumatic brain injury, while four weeks after Fpr1promoted differentiation of neuronal stem cells into neurons and reduced their differentiation into astrocytes via PI3K/Akt pathway.

Conclusions: Collectively, our study reported that immediately after TBI Fpr1increased acute inflammation, while after four weeks Fpr1promoted neurogenesis.