Longitudinal Outcome Of Fractalkine Receptor Deletion Up To One Year After Single Severe Traumatic Brain Injury In Mice

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Argomento: Neuroanestesia e neurorianimazione

The delayed nature of neuroinflammation after traumatic brain injury (TBI) sparks interest on inflammatory cells as targets for reducing disease burden. The receptor for the chemokine fractalkine (CX3CR1, selectively expressed in myeloid cells) is critical for microglial function and migration/recruitment of circulating immune cells to the site of injury [1,2]. Targeting the inflammatory response via deletion of one allele of CX3CR1 has been shown to confer protection in mice at one year post-TBI [3]. Homozygous CX3CR1 deletion however results in early brain protection followed by detrimental effects at one month post-TBI [4].

Purpose:

To investigate longitudinal effects on functional outcome in CX3CR1 Knock-Out (KO) mice up to one year survival after TBI.

Methods:

Wild type (WT) and CX3CR1 KO C57Bl/6 mice were subjected to sham or controlled cortical impact brain injury. Sensorimotor and cognitive deficits were longitudinally assessed by neuroscore, beam walk and novel object recognition (NOR) tests up to one year. Structural damage was evaluated by magnetic resonance imaging (MRI) at 12 months.

Results:

At chronic stages up to one year survival from TBI, CX3CR1 KO mice showed more severe sensorimotor deficits compared to WT mice. Beam walk test showed no difference in number of foot faults between WT and CX3CR1 KO mice. Compared to WT sham mice, both WT and CX3CR1 KO TBI mice showed cognitive deficits at NOR evaluation at 4 but not at 12 months. No difference was observed between WT and CX3CR1 KO mice. Structural damage assessed by MRI showed similar lesion volume in WT and CX3CR1 KO TBI mice.

Conclusions:

Our data show that CX3CR1 deletion may negatively affect long term outcome with a selective effect on sensorimotor function. Data suggest that fractalkine (CXCL1) signaling via CX3CR1 receptor may playa role in facilitating long-term recovery and repair after TBI