

Response of group 2 innate lymphoid cells (ILC2s) and pain measures in a mouse model of mild Traumatic Brain Injury

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Background

Mild Traumatic Brain Injury (TBI) is a global public health problem that can lead to significant post-injury complications, including headache, anxiety and cognitive issues. Despite this, very little is known about the underlying biology driving symptoms. Membranes surrounding the brain, called the meninges, are a candidate for mediating symptoms after mild TBI. Within the meninges, Group 2 innate lymphoid cells (ILC2s) are important for type 2 (Th2) immunity. Recent research shows meningeal ILC2-derived cytokines are important for brain function, therefore we tested meningeal ILC2 responses and pain after mild TBI.

Methods

We used a closed-head mouse model of mild TBI with head impact at the midline, caudal to bregma, at a speed of 5mm/sec and 5mm depth. Male and female wild type C57BL/6, Red5 IL-5 and IL-13eGFP reporter mice were used to interrogate Th2 cytokine production. Mice underwent a single mild TBI or sham procedure and three days of mechanosensitivity testing via periorbital Von Frey Test. Three days after injury, meninges were isolated and processed for multi-parameter flow cytometry and immunofluorescent imaging of immune cells and calcitonin gene-related peptide (CGRP) neurons.

Results and Conclusion

A single mild TBI reduced the numbers meningeal ILC2s, whilst increasing their activation and cytokine IL-5 and IL-13 expression. Mild TBI also increased ILC2-dependent granulocyte numbers, such as eosinophils and mast cells. Th2 readouts were more pronounced in female mice as was mechanical sensitivity. Immunofluorescent imaging suggests that IL-5 producing ILC2s co-localise with mast cells and CGRP+ nociceptive neurons following mild TBI. Therefore, we show that ILC2-mediated Th2 responses are altered meninges in the early phase after mild TBI and may be associated with mechanical sensitivity. Future work will test if Th2 cytokine responses can be modulated to affect pain measures after mild TBI.