ECB 2025 Conference
The 3rd International Electronic Conference on Biomedicines
12–15 May 2025 | Online
MDPI

Study of Hematopoiesis in Brain Trauma: Exploring New Approaches to Regulating Neuroinflammation and Neurogenesis

Alexander Dygai, Edgar Pan, Natalia Ermakova, Mariia Zhukova, Valentina Pan, Irina Zharkikh, Victoria Skurikhina
Institute of General Pathology and Pathophysiology, 125315 Moscow, Russia

INTRODUCTION & AIM

Approximately 10 million cases of traumatic brain injury (TBI) are reported worldwide annually, and this number continues to rise. The primary causes of TBI include road traffic accidents, falls, acts of violence, and contact sports. TBI is most frequently observed in young men, children, and individuals over 75 years of age [1]. TBI not only affects brain neurons but also triggers neuroinflammation and demyelination in white matter regions. These processes significantly increase the long-term risk of neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, chronic traumatic encephalopathy, and others.

Current treatments for traumatic brain injury (TBI) commonly focus on symptom management and lack strategies to prevent or delay the development of neurodegenerative processes. The lack of understanding of TBI mechanisms hinders the development of effective and safe approaches for anti-inflammatory therapy and the stimulation of regeneration in damaged and/or lost neurons.

The findings from the study of the blood system in traumatic brain injury (TBI) could provide novel biomarkers for the development of neurodegenerative processes, as well as approaches to modulating neuroinflammation and promoting neuroregeneration.

The aim of the study was to investigate the role of the blood system in the development of neuroinflammation and neurodegeneration in ICR mice after traumatic brain injury (TBI), as well as the potential of the sympatholytic reserpine to modulate neuroinflammation.

METHOD

Male ICR mice 12-14 weeks old were used in the experiment. Traumatic brain injury was induced by focal impact using a weight-drop model [2]. Neurological status of the mice was assessed before and at 6 hours, as well as on days 1, 3, 7, 14, 21, and 42 post-injury. Histological examination (hematoxylin and eosin staining), immunohistochemical staining, and analysis of the expression of astrocyte, mature, and immature neuron markers in the brain were performed. The content of hematopoietic cells in the blood and bone marrow was studied staining by the May-Grünwald-Giemsa staining method, along with the quantitative and qualitative composition of hematopoietic niches [3]. Additionally, in vitro analysis of hematopoietic and progenitor cells was performed. The sympatholytic drug reserpine was used to modulate neuroinflammation and neurogenesis.

RESULTS & DISCUSSION

Histological examination of mouse brain sections (H&E staining) demonstrated that impact at the bregma point caused:

Structural damage:

- Lesions in primary/secondary motor cortex and motor-sensory cortex (**Fig. 1**).
- Disruption of the vascular network, tissue edema (**Fig. 1**).

Cellular responses:

- Neuroinflammation, cell degeneration (peak at 6th hour, 3rd and 42nd day post-TBI) (**Fig. 1**).
- Astrogliosis and glial scar formation (**Fig. 1**).

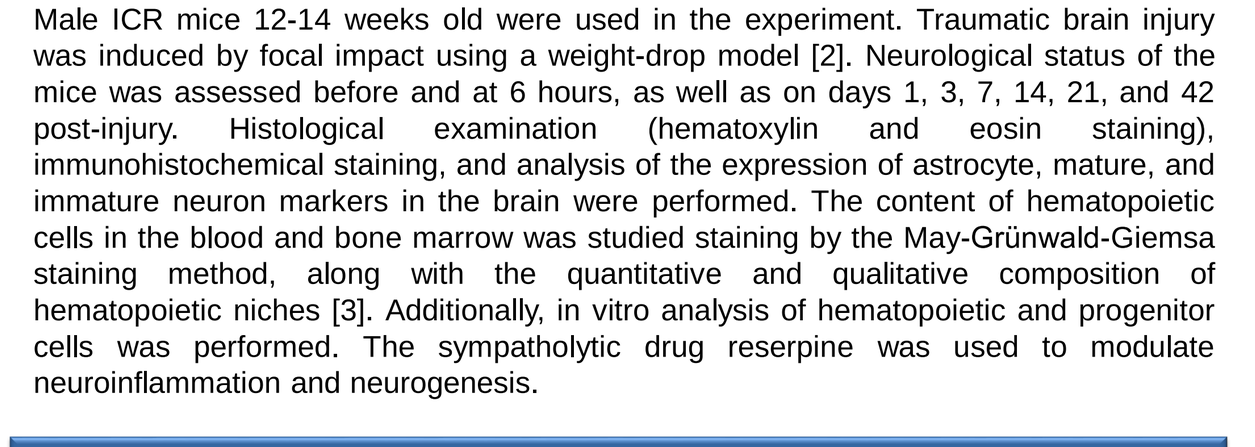

Figure 1: Histological structure of the motor cortex in male ICR mice. Hematoxylin and eosin (H&E) staining, ×100. A – Intact control; B – 6th hour post-TBI; C – 3rd day post-TBI; D – 42th days post-TBI.

Immunohistochemical staining revealed key post-TBI alterations at 3rd and 21st day post-TBI:

Neurogenesis impairment:

- Decreased DCX-expressing proliferating neuroblasts in the subventricular zone (**Fig. 2**).
- Increased NeuN-expressing mature neurons in subventricular zone (**Fig. 2**).

Changes in astrocyte content:

- Reduced GFAP-expressing cell counts, indicating impaired migration (**Fig. 2**).

The $DCX^+/NeuN^+$ expressing cells shift post-TBI indicates impaired neuroblast proliferation via premature differentiation, likely reducing SVZ regenerative potential and promoting neurodegeneration.

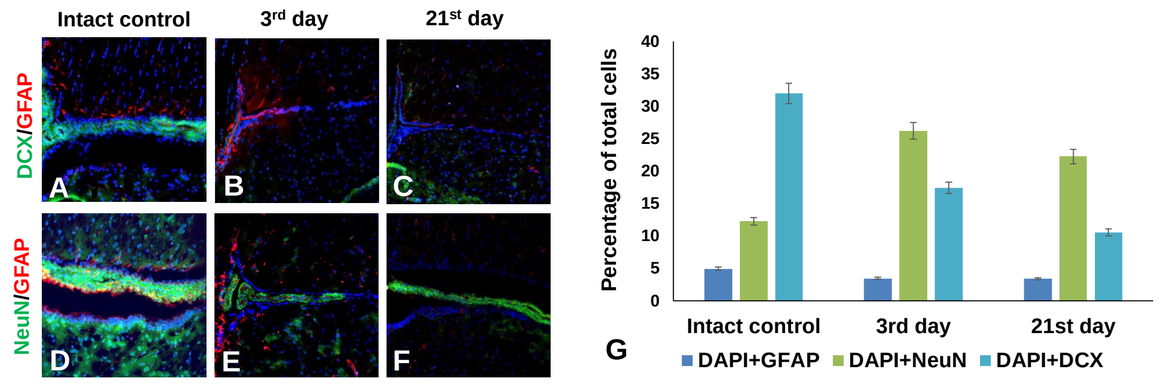

Figure 2: Immunofluorescence images of the subventricular zone (A-F) in the brain of male ICR mice. Neuroblasts are stained with anti-DCX antibodies (green) (A-C), mature neurons with anti-NeuN antibodies (green) (D-F), astrocytes with anti-GFAP antibodies (red) (A-F), and cell nuclei with the fluorescent dye DAPI (blue). Magnification: ×200. A, D – intact control; B, E – 3 days post-TBI; C, F – 21 days post-TBI. G - Relative abundance of neurons, neuroblasts and glial cells (% of total DAPI-stained cells) in the subventricular zone of mice brain.

Blood System Analysis & Reserpine Effects:

TBI-induced changes:

- An increase in the number of hematopoietic progenitor cells in the bone marrow (**Fig. 3**).
- Peripheral blood leukocytosis (**Fig. 4**).
- Fluctuations in the total number of leukocytes (WBC) (**Fig. 4**).

Reserpine effects (1 mg/kg day 3 + 0.1 mg/kg days 4–7):

- Decreased karyocytes in bone marrow (**Fig. 3**).
- ~20-30% reduction in WBC count (**Fig. 4**).

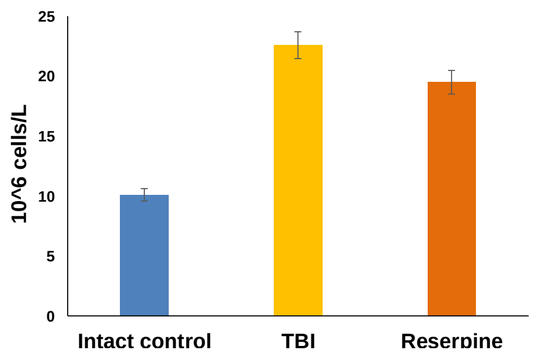

Figure 3: Total karyocyte count in the bone marrow of ICR mice post-TBI and reserpine treatment.

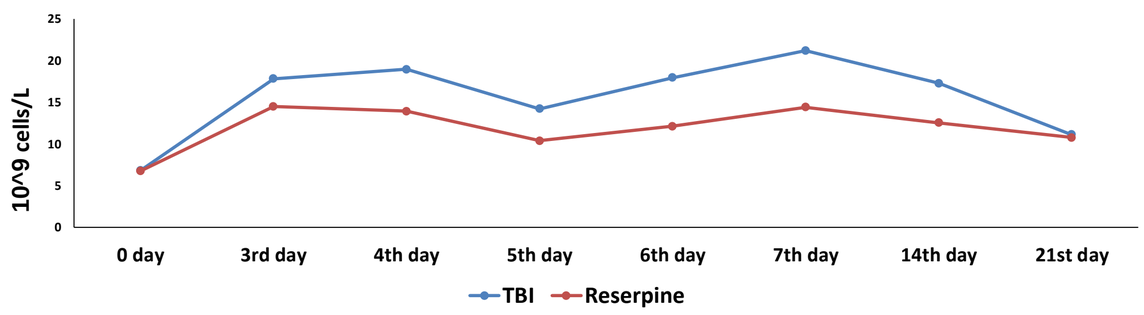

Figure 4: Total Leukocyte Count (TLC) fluctuations in the blood of ICR mice post-TBI and reserpine treatment.

CONCLUSION

The observed changes suggest a link between leukocytosis and neuroinflammation. They indicate that blood leukocytes may serve as biomarkers of TBI severity and underscore reserpine's ability to modulate the blood system's response to TBI. These findings imply that pharmacological blockade of the sympathetic regulation of hematopoiesis could form a basis for novel therapeutic strategies to mitigate neuroinflammation and enhance neuroregeneration following TBI.

FUTURE WORK / REFERENCES

1) Mira, R. G., Lira, M., & Cerpa, W. (2021). Traumatic Brain Injury: Mechanisms of Glial Response. Frontiers in physiology, 12, 740939. https://doi.org/10.3389/fphys.2021.740939
2) Chakraborty, N., Hammamieh, R., Gautam, A., Miller, S. A., Condlin, M. L., Jett, M., & Scrimgeour, A. G. (2021). TBI weight-drop model with variable impact heights differentially perturbs hippocampus-cerebellum specific transcriptomic profile. Experimental neurology, 335, 113516. https://doi.org/10.1016/j.expneurol.2020.113516
3) Crocker, P. R., & Gordon, S. (1985). Isolation and characterization of resident stromal macrophages and hematopoietic cell clusters from mouse bone marrow. The Journal of experimental medicine, 162(3), 993–1014. https://doi.org/10.1084/jem.162.3.993