SIGMA-1 RECEPTORS IN THE PATHOGENESIS OF CEREBROHEPATIC DISORDERS IN TRAUMATIC BRAIN INJURY: CURRENT STATE OF THE PROBLEM

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BACKGROUND

Traumatic brain injury (TBI) is a major medical and social problem, as its consequences may be accompanied by systemic dysfunction of internal organs. The liver plays a key role in metabolism, biotransformation of xenobiotics, regulation of inflammatory responses, and maintenance of metabolic homeostasis.



OBJECTIVE

To summarize current scientific evidence on the mechanisms underlying cerebrohepatic disorders following TBI and to identify promising directions for investigating the pathogenetic role of sigma-1 receptors (σ1R).

CLINICAL RELEVANCE

- After TBI, systemic inflammation, oxidative stress, impaired microcirculation and neurohumoral dysregulation may contribute to secondary liver injury.
- Metabolic and inflammatory changes in the liver may, in turn, influence the course of post-traumatic CNS dysfunction.

KEY MECHANISMS

Important factors in the pathogenesis of secondary brain and liver injury:

- ROS ↑ Oxidative stress
- Imbalance of pro- and anti-inflammatory mediators
- Mitochondrial dysfunction and impaired energy metabolism
- Alterations in cellular mechanisms of stress adaptation

These factors may form bidirectional pathological communication between the central nervous system and the liver.

TRAUMATIC BRAIN INJURY



BRAIN

- Neuroinflammation
- Oxidative stress
- Mitochondrial dysfunction
- Neuronal injury

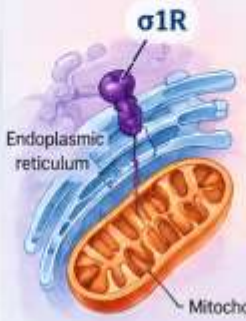
Regulation of Ca^{2+} homeostasis
Mitochondrial function
Endoplasmic reticulum stress response
Cell survival

LIVER

- Inflammatory response
- Hepatocyte cytolysis
- Metabolic disturbances
- Impaired detoxification

ROLE OF σ1R

Sigma-1 receptors are ER-resident proteins involved in:



- Regulation of intracellular calcium homeostasis
- Mitochondrial function
- Endoplasmic reticulum stress response
- Cell survival
- Adaptive responses under ischemic, inflammatory and traumatic conditions

PERSPECTIVE DIRECTIONS

- Study of σ1R expression in brain and liver at different time points after TBI
- Correlation with markers of oxidative stress, inflammation, hepatocyte cytolysis and organ function
- Evaluation of pharmacological modulation of σ1R (e.g., selective agonist PRE-084)
- Experimental verification of potential cytoprotective effects, considering the cerebrohepatic system as a whole

CONCLUSIONS

- Cerebrohepatic disorders following TBI represent a promising area of experimental pathophysiology.
- Sigma-1 receptors are a potential molecular target for studying mechanisms of cellular adaptation and cytoprotection.
- Further investigation of their expression and functional role in the brain and liver, as well as the effects of pharmacological modulation, may contribute to a deeper understanding of the pathogenesis of post-traumatic cerebrohepatic disorders.