MOLECULAR MECHANISMS OF BRAIN–HEART INTERACTION IN TRAUMATIC BRAIN INJURY: THE ROLE OF SIGMA-1 RECEPTORS

Sikora K.V., Kmet T.I.
Bukovinian State Medical University, Chernivtsi, Ukraine
Department of Hygiene and Ecology



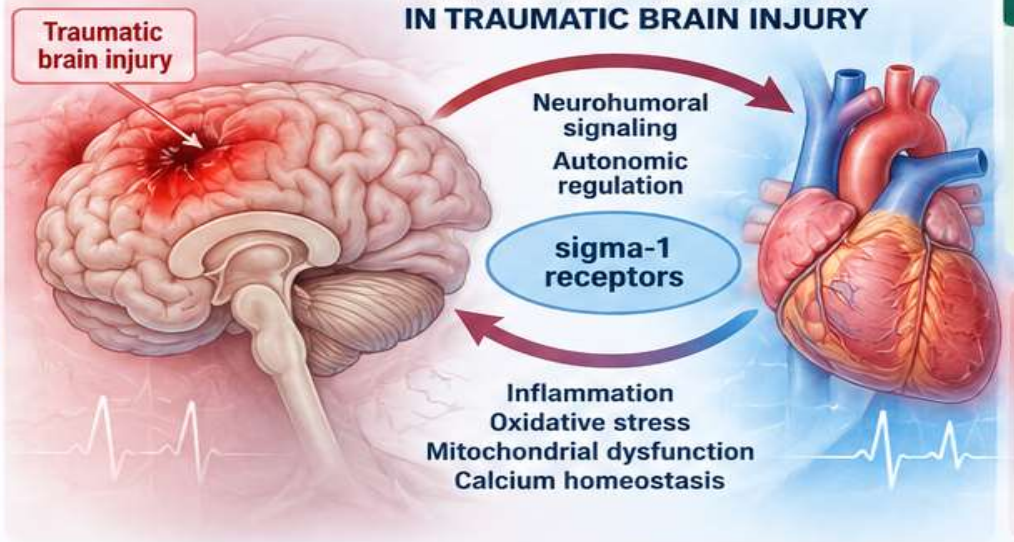
BACKGROUND

Traumatic brain injury (TBI) is an important medical and social problem. Its consequences extend beyond primary brain damage and are accompanied by systemic disorders, particularly cardiovascular dysfunction. Cerebrocardiac disturbances after TBI may manifest as alterations in cardiac rhythm, myocardial electrical activity, autonomic regulation and biochemical markers of cardiomyocyte injury.

AIM

To summarize current scientific evidence on the mechanisms of cerebrocardiac disturbances after TBI and to substantiate the potential of sigma-1 receptors (σ1R) as a promising pharmacological target.

BRAIN–HEART INTERACTION IN TRAUMATIC BRAIN INJURY



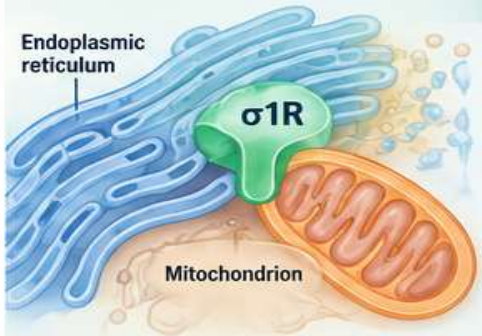
KEY MECHANISMS OF CEREBROCARDIAC DISTURBANCES AFTER TBI

- Dysfunction of central autonomic structures
- Excessive sympathoadrenal activation (catecholamines ↑)
- Neuroinflammation and oxidative stress
- Mitochondrial dysfunction
- Disturbed intracellular calcium homeostasis

CONSEQUENCES FOR THE HEART

- Arrhythmias
- Changes in heart rate and heart rate variability
- Increased metabolic load on the myocardium
- Oxidative damage of cardiomyocytes
- Biochemical markers of myocardial injury

SIGMA-1 RECEPTORS (σ1R)



MAIN FUNCTIONS

- Regulation of calcium homeostasis
- Modulation of mitochondrial function
- Cellular response to stress
- Regulation of intracellular signaling pathways

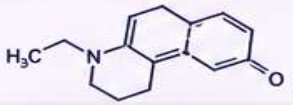
Located at the endoplasmic reticulum–mitochondria interface
Intracellular regulatory proteins

σ1R may enhance cellular resistance to damaging factors in both neurons and cardiomyocytes.

PHARMACOLOGICAL MODULATION

PRE-084

Selective sigma-1 receptor agonist



POTENTIAL EFFECTS IN TBI

- Neuroprotective effects
- Cardioprotective effects
- Reduction of inflammation and oxidative stress
- Improvement of mitochondrial function and calcium homeostasis

The effects of PRE-084 require experimental confirmation.

PERSPECTIVES OF RESEARCH

- Assessment of σ1R expression and functional state in brain structures and myocardium
- Correlation with indices of autonomic regulation and electrocardiographic changes
- Analysis of markers of myocardial injury, oxidative stress and inflammation
- Evaluation of the effects of PRE-084 on cardiac function, structural changes in the myocardium and brain, and biochemical markers

Changes in receptor expression alone are not sufficient evidence of their pathogenetic role. Pharmacological modulation of σ1R complements morphological and biochemical studies.

CONCLUSIONS

1. Cerebrocardiac disturbances after TBI result from the interaction of neurogenic, neurohumoral and cellular-molecular mechanisms, including autonomic dysregulation, oxidative stress, neuroinflammation and mitochondrial dysfunction.
2. Sigma-1 receptors, through their role in regulation of intracellular calcium homeostasis and cellular stress responses, are a promising target for investigating the mechanisms of post-traumatic brain and cardiac injury.
3. Comprehensive assessment of σ1R expression and the effects of their pharmacological modulation using PRE-084 may deepen our understanding of the pathogenesis of cerebrocardiac disturbances and provide a basis for the development of new approaches to their correction.