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c-Jun N-terminal kinases (JNKs) in myocardial and cerebral ischemia/reperfusion injury

Shvedova M., Anfinogenova Y., Atochina-Vasserman E., Schepetkin I., Atochin D.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2018 Shvedova, Anfinogenova, Atochina-Vasserman, Schepetkin and Atochin. In this article, we review the literature regarding the role of c-Jun N-terminal kinases (JNKs) in cerebral and myocardial ischemia/reperfusion injury. Numerous studies demonstrate that JNK-mediated signaling pathways play an essential role in cerebral and myocardial ischemia/reperfusion injury. JNK-associated mechanisms are involved in preconditioning and post-conditioning of the heart and the brain. The literature and our own studies suggest that JNK inhibitors may exert cardioprotective and neuroprotective properties. The effects of modulating the JNK-depending pathways in the brain and the heart are reviewed. Cardioprotective and neuroprotective mechanisms of JNK inhibitors are discussed in detail including synthetic small molecule inhibitors (AS601245, SP600125, IQ-1S, and SR-3306), ion channel inhibitor GsMTx4, JNK-interacting proteins, inhibitors of mixed-lineage kinase (MLK) and MLK-interacting proteins, inhibitors of glutamate receptors, nitric oxide (NO) donors, and anesthetics. The role of JNKs in ischemia/reperfusion injury of the heart in diabetes mellitus is discussed in the context of comorbidities. According to reviewed literature, JNKs represent promising therapeutic targets for protection of the brain and the heart against ischemic stroke and myocardial infarction, respectively. However, different members of the JNK family exert diverse physiological properties which may not allow for systemic administration of non-specific JNK inhibitors for therapeutic purposes. Currently available candidate JNK inhibitors with high therapeutic potential are identified. The further search for selective JNK3 inhibitors remains an important task.

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Keywords

Brain, C-Jun-N-terminal kinase, Heart, Ischemia/reperfusion injury, JNK inhibitor, Stroke

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