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Activation of prosurvival signaling pathways during the memory phase of volatile anesthetic preconditioning in human myocardium: a pilot study

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Abstract According to a compelling body of evidence anesthetic preconditioning (APC) attenuates the deleterious consequences of ischemia–reperfusion and protects the heart through a mechanism similar to ischemic preconditioning. The present study was purported to investigate the intracellular signaling pathways activated in human myocardium in response to a preconditioning protocol with two different volatile anesthetics, namely isoflurane and sevoflurane. To this aim, phosphorylation of PKCα and -δ, ERK1/2, Akt, and GSK3β was determined at the end of the APC protocol, in human atrial samples harvested from patients undergoing open-heart surgery. The results demonstrate that preconditioning with volatile anesthetics triggers the activation of PKCδ and -α isoforms and of prosurvival kinases, ERK1/2, and Akt, while inhibiting their downstream target GSK3β during the memory phase.

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Introduction

Ischemia/reperfusion (I/R) injury due to acute coronary syndromes and heart surgery represents currently a leading cause of cardiac morbi-mortality and an increasing burden for healthcare systems worldwide. The loss of blood supply to myocardium causes progressive cellular damage that eventually leads to cell death. Tissue damage occurs as a result of the initial ischemic episode and is mainly determined by its duration, whereas cell death occurs during reperfusion. Brief episodes of ischemia and reperfusion render the heart more tolerant to a subsequent prolonged ischemic insult, a phenomenon known as ischemic preconditioning [1]. Ischemic preconditioning (IPC) is the most powerful innate mechanism reported to protect against myocardial ischemic injury by reducing infarct size, attenuating the incidence and severity of reperfusion-induced arrhythmias, and preventing endothelial cell dysfunction in every species tested, including humans [2, 3]. However, preconditioning-like protection can be activated not only by short ischemic insults, but also by brief application of pharmacological agents or volatile anesthetics [4, 5]. With respect to the latter, preconditioning with volatile anesthetics (anesthetic preconditioning or APC) is equally effective in protecting the myocardium from I/R injury and, also in preventing ischemic cardiac dysfunction in the perioperative period [6, 7]. Moreover, IPC and APC have also been shown to recruit similar intracellular signal transduction pathways in both in vitro and in vivo experimental models. Indeed, several kinases such as protein kinase C (PKC), ERK1/2 mitogen-activated

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