Chronic pain and cardioprotection

Abstract:

Myocardial infarction is the leading cause of death in the world. Restored blood flow quickly is the most effective way to rescue myocardium but also caused ischemia-reperfusion (IR) injury. Some studies indicated that brief episodes of ischemia at a distant organ could reduce the myocardial reperfusion injury. This is so called remote ischemic preconditioning (RIPC) cardioprotection. Several circulating factors and neurogenic signals contribute to the cardioprotection by RIPC. Acute pain has been shown to decrease myocardial IR injury. However, whether pre-existing chronic pain is deleterious or protective to cardiac IR injury is unclear. To answer this question, we used mice subjected to spared nerve injury (SNI) surgery to induce chronic neuropathic pain. After the development of chronic pain (5 days after SNI surgery), mice were subjected to left anterior descending artery occlusion for 45 min and allowed for reperfusion for 24 hours to induce myocardial IR injury. The results showed that mice with SNI-induced chronic pain had reduced IR injury compared to those of sham-operated group. Furthermore, SNI-induced cardioprotection is mediated via a known cardioprotective PKC-dependent pathway. We have shown that ERK activation in anterior part of paraventricular nucleus of the thalamus (PVA) is required for the development of chronic pain. To test the involvement of PVA ERK activation in SNI-induced cardioprotection, U0126 or PDBu were used to block or activate ERK activity in PVA, respectively. We found that blocking ERK activity abolished the SNI-induced cardioprotection. On the other hand, activation of ERK in PVA in naïve mice is enough to elicit cardioprotection. To investigate the role of autonomous nerve system in SNI-induced cardioprotection, blockers of parasympathetic (glycopyrrolate) or sympathetic (propranolol) nerves were used. The results showed that inhibition of parasympathetic nervous system abolished SNI-induced the cardioprotection. These findings demonstrate chronic neuropathic pain protects myocardial reperfusion injury through ERK activation in PVA.