Eur J Pain. 2014 Nov;18(10):1458-70. doi: 10.1002/ejp.511. Epub 2014 Apr 22.

Resveratrol reduces morphine tolerance by inhibiting microglial activation via AMPK signalling.

Han Y[1], Jiang C, Tang J, Wang C, Wu P, Zhang G, Liu W, Jamangulova N, Wu X, Song X.

Author information

Abstract

BACKGROUND: Evidence has accumulated indicating that microglia within the spinal cord play a critical role in morphine tolerance. The present study investigated the effects and possible mechanisms of 5' adenosine monophosphate-activated protein kinase (AMPK) activator resveratrol and AICAR to inhibit microglial activation and to limit the decrease in antinociceptive effects of morphine.

METHODS: The microglial cell line BV-2 was used. Cytokine expression was measured using quantitative polymerase chain reaction. Cell signalling was assayed by Western blot and immunohistochemistry. The antinociception and morphine tolerance were assessed in CD-1 mice using the hot plate and tail-flick tests.

RESULTS: (1) Morphine induces robust BV-2 cell activation, as evidenced by increased p38 mitogen-activated protein kinase phosphorylation, nuclear factor-κB translocation and mRNA expression of pro-inflammatory cytokines [including interleukin-1β (IL-1β), IL-6 and tumour necrosis factor-α], inducible nitric oxide synthase and Toll-like receptor-4, and these changes are inhibited by resveratrol. (2) Resveratrol activates AMPK to suppress morphine-induced BV-2 cell activation. AICAR, another AMPK activator, can mimic the effects of resveratrol, whereas compound C, an AMPK inhibitor, reverses the inhibitory effects of resveratrol treatment. (3) Systemic or spinal administration of resveratrol with morphine significantly blocks microglial activation in the spinal cord and then attenuates the development of acute and chronic morphine tolerance in both male and female mice.

CONCLUSION: Resveratrol directly suppresses morphine-induced microglial activation through activating AMPK, resulting in significant attenuation of morphine antinociceptive tolerance.

PMID: 24756886 [PubMed - indexed for MEDLINE]

0 comments

How to join PubMed Commons