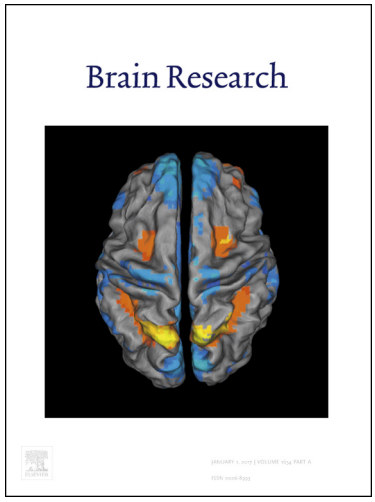

Research report

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Nasim Sadat Pajohanfar, Ehsan Mohebbi, Abolfazl Rad, Akbar Pejhan, Samad Nazemi, Bahareh Amin

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Protective effects of atorvastatin against morphine-induced tolerance and dependence in mice

Nasim Sadat Pajohanfar[1], Ehsan Mohebbi[1], Abolfazl Rad[2], Akbar Pejhan[3], Samad Nazemi[3], Bahareh Amin [3,*]

[1] Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran
[2] Cellular and Molecular Research Center, Department of Biochemistry and Nutrition, Sabzevar University of Medical Sciences, Sabzevar, Iran

[3,*] Correspondence
Cellular and Molecular Research Center, Department of Physiology and Pharmacology, Faculty of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran, Tel.: +985144264462, Fax: +985144264462, E-mail: aminb@medsab.ac.ir

Abstract

Background: In this study, we evaluated the effects of atorvastatin, a lipid-lowering medication on morphine-induced tolerance and dependence in mice.

Methods: Tolerance was induced by subcutaneous administration of morphine (20 mg/kg) to animals, twice a day for 9 days. Atorvastatin was given at the doses of 5, 10 and 20 mg/kg, 30 min before each morphine administration, once daily for 9 days. Hot plate test was employed to assess antinociceptive effect of morphine on days 1, 3, 5, 7 and 9. Dependence was evaluated by naloxone-precipitated withdrawal syndrome. We attempted to verify withdrawal regulation of induced nitric oxide synthase (iNOS), astroglia marker, glial fibrillary acidic protein (GFAP), ionized calcium-binding protein (Iba1), a microglia activation marker, a pro-inflammatory mediator, tumor necrosis alpha (TNF-α) and immune receptor, toll like receptor 4 (TLR-4) genes by real-time polymerase chain reaction (RT-PCR). Lipid peroxidation was estimated by assessing malondialdehyde (MDA) content in the spinal cord of animals