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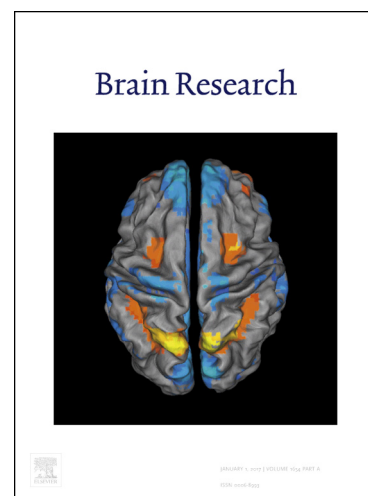
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Protective effects of atorvastatin against morphine-induced tolerance and dependence in mice

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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

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