

Count: 175

Abstract ID: 245

subject: Emotion, Motivation
and Behavior: Reward and the Brain

Presentation Type: Oral

Effect of silver nanoparticles on expression of naloxone- induced withdrawal symptoms in the morphine conditioned rat

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Background and Aim : Drug seeking behavior is a complex phenomenon which can be displayed by animals. Repeated injection of morphine make the rat conditioned to place while naloxone, a competitive opioid receptor antagonist, may reverse the effect of morphine. Nanomaterials (NMs) are materials that have structural components smaller than 1 μm in at least one dimension. Silver nanoparticles, one of the most commercially used nanomaterials, may be available in biological systems because that the use and degradation of nanosilver-impregnated products will likely result in an environmental release of nanosilver. The purpose of this research was to study the effects of silver nanoparticle on naloxone induced withdrawal behavioral signs in morphine conditioned rats.

Methods : Animals (male Wistar rats weighing 300-350 g) were cannulated bilaterally by stereotaxis apparatus for the CeA (Anteriorposterior= -2.28 mm posterior to bregma and lateral= ± 4.1 mm; dorsoventral= 7.8 mm, according to the atlas of Paxinos and Watson (Paxinos and Watson 2007) coordinates and passed a recovery period lasting one week. Conditioned place preference was conducted using a five-day schedule of an unbiased procedure including three phases (pre-conditioning, conditioning, and test). Morphine (2.5-10 mg/kg) was injected subcutaneously (s.c) through the conditioning once a day. On test day, naloxone (0.05- 0.4 $\mu\text{g}/\text{rat}$) was administrated intra- central nucleus of amygdala (CeA) 5 min before testing. Silver nanoparticles (0.0001, 0.001, 0.01 $\mu\text{g}/\text{rat}$) were injected intra-nucleus 15 min before microinjection of naloxone (0.4 $\mu\text{g}/\text{rat}$). The behavioral signs was recorded and assessed by Ethovision system. Behavioral data in all groups were compared by ANOVA (one- and/or two-way analysis of variance).

Basic and Clinical
**6th NEUROSCIENCE
Congress 2017**

December, 20-22 2017 Razi Hall, Tehran, Iran



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Results : Morphine repeated injection (5 mg/kg, s.c.) induced a significant drug-seeking behaviors in experimental animals compared with the control group. Naloxone microinjection into CeA (0.4 μ g/rat) did not cause meaningful withdrawal response. But, a microinjection of silver nanoparticles (0.001, 0.0001 μ g/rat) had significant effect on expression of naloxone- induced withdrawal symptoms in the morphine conditioned rat while the single particles (intra-CeA) did not provide significant signs.

Conclusion : The silver nanoparticles in the CeA may augment the antagonistic effect of Naloxone pre-testing of place conditioning of rats to morphine.

Keywords : morphine, naloxone, silver nanoparticles, withdrawal, rat