Morphine withdrawal anxiety influenced by pituitary adenylate cyclase-activating polypeptide (PACAP) in mice

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Introduction: In this study the effect of PACAP on morphine withdrawal anxiety was investigated in mice. The elevated plus maze (EPM) and jump-test were used to assess morphine withdrawal anxiety. Morphine withdrawal is known to be anxiogenic in rats. In contrast to rats, in our research naloxone precipitated withdrawal induced anxiolytic effect.

Methods: CFLP male mice were used. Mice were treated twice daily with s.c. injections of morphine or saline and once daily with PACAP (500 ng/2 μl, i.c.v.) or ACSF. Treatments for EPM: day 1: 10 mg/kg, day 2: 20 mg/kg, day 3: 40 mg/kg; final dose day 4: 20 mg/kg. Treatments for jump-test: day 1: 20 mg/kg, day 2: 40 mg/kg, day 3: 60 mg/kg, day 4: 80 mg/kg, final dose day 5: 100 mg/kg. Results: EPM: naloxone (0.2 mg/kg, s.c.) administration in morphine dependent mice significantly increased the open-arm time/total time rate and the number of entries in arms compared with the control mice. PACAP had no significant effect on open-arm time/total time rate, but significantly increased the total number of entries compared with the naloxone precipitated withdrawal morphine-dependent mice. Jump-test: after naloxone (1 mg/kg, s.c.) injection, morphine-dependent mice treated with PACAP exhibited significant decrease in jumping behavior and significant increase body temperature compared morphine dependent mice. Conclusion: PACAP compensated the effects of morphine withdrawal; these results may help us to understand morphine withdrawal anxiety.

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