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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:** C57BL/6J 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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