



## Involvement of adenosine receptor agonists on the development of hypersensitivity to acute dose of morphine during morphine withdrawal period

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### Abstract:

In the present study, the involvement of the selective adenosine  $A_1$  (CPA) and  $A_{2A}$  (CGS 21680) and non-selective adenosine  $A_1/A_{2A}$  (NECA) receptor agonists on the development of hypersensitivity to acute morphine injection given during opiate withdrawal was investigated. Intraperitoneal (*ip*) injections of morphine at increasing doses (10, 20, 30, 40, 50 mg/kg) for 6 consecutive days produced a state of dependence. On the 6th day, in the morning, animals were injected with the last dose of morphine (50 mg/kg, *ip*). Each day, 20 min before each injection of morphine, adenosine receptor agonists were also administered. Seven days after cessation of the morphine treatment, on the 13th day of the experiment, all animals were challenged with a dose of morphine (10 mg/kg, *ip*). A clear increase in locomotor activity was observed, indicating that hypersensitivity had developed. Our study has demonstrated the presence of an attenuating effect of adenosinergic drugs, such as CGS 21680 and NECA, but not CPA, on the development of hypersensitivity. The results indicate that stimulation of the adenosine  $A_{2A}$  receptor plays some role in modulating the neuroadaptive changes appearing during chronic opioid treatment and that adenosine  $A_{2A}$  receptor agonists may serve as useful drugs in relapse protection. Our investigations focused on adenosine  $A_{2A}$  agonists as possible vehicles for pharmacotherapy for morphine addiction.

### Key words:

adenosine receptor agonists, morphine withdrawal signs, hypersensitivity

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