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Involvement of D1/D2 dopamine receptors within the nucleus accumbens and ventral tegmental area in the development of sensitization to antinociceptive effect of morphine

Leila Zarepour
Iran University of Medical Science, Iran

The nucleus accumbens (NAc) and the ventral tegmental area (VTA) are two major areas for the mesolimbic dopaminergic system, which are strongly involved in the development of behavioral sensitization. In the present study, we investigated the role of D1/D2 dopaminergic receptors within the NAc or VTA in response to sensitization to morphine by the tail-flick test as a model of acute pain. Sensitization was induced by subcutaneous (SC) injection of morphine (5 mg/kg), once daily for three days followed by five days free of drug. After the sensitization period, antinociceptive responses induced by an ineffective dose of morphine (1 mg/kg; SC) were obtained by the tail-flick test and represented as maximal possible effect (%MPE). In experimental groups, D1 and D2 receptor antagonists, SCH-23390 and sulpiride (0.25, 1 and 4 µg/rat), were separately microinjected into the NAc or VTA, 10 minutes before morphine administration during the sensitization period, respectively. Results showed that, injection of morphine during the sensitization period (development of sensitization) increased %MPE of the ineffective dose of morphine from 2.43±1.4% in naive to 47.75±4.01% in sensitized animals ($P<0.001$). Unilateral microinjections of different doses of the D1/D2 receptor antagonists, SCH-23390 and sulpiride, into the NAc dose-dependently decreased %MPEs in morphine-sensitized animals. Nonetheless, %MPEs were only affected by intra-VTA administration of SCH-23390 in morphine-sensitized animals ($P<0.05$). Our findings suggest that both the D1/D2 dopamine receptors in the NAc and the D1 receptors in the VTA may be of more important in the development of sensitization to in rats.

leilazarepour1@yahoo.com

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