



**Central endothelin-B receptor stimulation does not affect morphine analgesia in rats.**

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Several neurotransmitter mechanisms have been proposed to play a role in the actions of morphine. We reported that centrally administered endothelin A (ETA) receptor antagonists potentiate morphine analgesia in rats. It has also been reported that ETB agonist, IRL1620, has antinociceptive action mediated through opiate receptors in the periphery. The present study was conducted to determine if central ETB receptors are involved in analgesic actions of morphine. The effect of intracerebroventricular (i.c.v.) administration of ETB receptor agonist, IRL1620, on morphine-induced analgesia and hyperthermia was determined in the rat. Morphine (4 mg/kg, s.c.) produced a significant increase (84%) in tail-flick latency compared to the control group and the analgesic response lasted for 4 h. IRL1620 (30 microg, i.c.v.) did not produce any increase (16%) in tail-flick latency over the 5-hour observation period in vehicle-treated rats. Pretreatment with IRL1620 (3, 10, and 30 microg, i.c.v.) did not have any significant effect on the intensity and duration of morphine (4 mg/kg, s.c.)-induced analgesia. Morphine (4 mg/kg, s.c.) administration produced an increase in body temperature compared to the control group. In vehicle-pretreated rats, IRL1620 (30 microg, i.c.v.) did not produce any change in body temperature. The morphine-induced hyperthermic effect was not altered in IRL1620-pretreated rats. These studies demonstrate that IRL1620, a specific ETB receptor agonist, did not affect the morphine-induced analgesic and hyperthermic effect in rats. It can be concluded that central ETB receptors are not involved in modulation of pharmacological actions of morphine.