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A selective antagonist of the CRF_1 Receptor, CP-154,526, antagonises the morphine-induced conditioned place preference and corticosterone release

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Corticotropin-releasing factor (CRF) plays a major role in regulating behavioural and hormonal responses to stress in animal models. It has been proposed that CRF system contributes in an important way at compulsive drug use. The aim of the present work was to evaluate the role of the selective CRF1 receptor (CRF1R) antagonist, CP154,526, in the rewarding effects of morphine, as well as in the possible changes in plasma corticosterone concentration, as hypothalamus-pituitary adrenal (HPA) axis activation marker. The rewarding effects of morphine were evaluated using the conditioning place preference (CPP) paradigm, in male Swiss strained mice. We gave a dose of CRF1R antagonist (i.p.) 30 minutes before morphine (s.c.) or saline (s.c.) administration. The four experimental conditions investigated were: Tween-80 (10%) + saline (n =6), Tween-80 (10%) + morphine (n =6), CP154,526 + saline (n =4), and CP154,526 + morphine (n =6). Data are presented as mean ± SEM. Data were analysed using two-way analysis of variance (ANOVA) followed by a post hoc Newman–Keul's test. Animals were weighted every day during the experiment. The CPP score was calculated for each mouse as the difference between time spent in the drug-paired compartment during the postconditioning and the preconditioning phase. Plasma levels of corticosterone were quantified by means of radioinmunoassay. Mice treated with morphine showed a significantly lower weight gain than animals receiving saline injection, which was not modified by CRF1R antagonist administration. Moreover, a significant rewarding effect of morphine was observed in the place conditioning paradigm, which was prevented by CP154,526. Moreover, morphine-induced CPP evoked an activation of the HPA axis, measured as corticosterone plasma levels, which was blocked by CP154,526. Our data suggest a main role of the CRF system, through CRF1R, in modulating the rewarding effects of morphine and in the CPP-induced HPA axis activation.