D_1 AND D_2 DOPAMINE AGONISTS PRODUCE CONTRASTING EFFECTS ON MU, KAPPA AND DELTA-OPIOID MEDIATED ANTINOCICEPTION

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Controversy exists concerning a dopaminergic involvement in opioid mediated antinociception. In this context stimulation of dopamine (DA) receptors in the central nervous system (CNS) has been shown to enhance (Dunai-Kovacs and Szekely 1977, Ben-Sreti et al 1983) and attenuate (Tulunay et al 1975) morphine induced antinociception. With respect to DA receptor antagonism, droperidol, a butyrophenone antipsychotic, has been shown to enhance antinociception induced by fentanyl and sufentanil but not that induced by morphine (Statile et al 1988). Since several types of opioid receptor, namely μ, k and δ, have been implicated in the mediation of opioid induced antinociception, it is possible that the extent by which specific dopaminergic mechanisms modulate the activity of opioids at their different receptor subtypes will influence the expression of the antinociceptive response. The aim of the current study was therefore to determine at the central level, the effects of the selective DA agonists quinpirole (D_2) and SKF38393 (D_1) on antinociception induced by sufentanil (μ), PD117302 (k) and D-ala^2-D-leu^5-enkephalin (DADL-δ).

In the mouse tail immersion test (Sewell and Spencer 1976) sufentanil (10μg kg $^{-1}$ip) and PD117302 (7mg kg^{-1}ip) antinociception was enhanced ($P<0.05$) by centrally administered quinpirole (100μg/animal). Peripheral administration of quinpirole (5mg kg^{-1}ip), however, was devoid of effect on μ and k antinociceptive activity but markedly ($P<0.05$) increased that of DADL (1μg/animal icv). In contrast SKF38393 (20μg/animal icv) attenuated ($P<0.05$) the antinociception induced by sufentanil and PD117302 but when given intraperitoneally, SKF38393 (1mg kg^{-1}) failed to modify nociceptive latencies induced by μ, k and δ opioid agonists.

Thus, the D_2 agonist quinpirole consistently enhanced the antinociception induced by μ, k and δ opioids at a central level. The converse was noted with SKF38393 D_1 agonism and μ and k but not δ activity. It must be noted however that the apparent lack of D_1/δ interaction could possibly be ascribed to the low dose of SKF38393 employed. In conclusion, therefore, there appears to be a complex interplay between dopaminergic and opioid systems in which D_2 stimulation facilitates, whilst D_1 stimulation attenuates opioid antinociception.

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