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## Antinociceptive Effects of Dopaminergic Agents in the Spinal Cord of the Rat

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*Phil. Trans. R. Soc. Lond. B* 1985 **308**, 429

doi: 10.1098/rstb.1985.0063

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## 23. Antinociceptive effects of dopaminergic agents in the spinal cord of the rat

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There is considerable evidence that activity in central dopaminergic pathways can affect an animal's responsiveness to noxious stimulation. For example, we have recently found that both the intravenous and intrathecal administration of the dopamine agonist apomorphine (APO) leads to an increase in the tail flick latency (t.f.l.) in the rat (Barasi & Duggal 1984). In the first part of the study we have further investigated the dopamine receptors involved in the mediation of this effect.

Experiments were performed on rats lightly anaesthetized with sodium pentobarbitone such that a reflex withdrawal of the tail was elicited in response to the application of noxious radiant heat. Various dopamine agonists were administered via an intrathecal cannula.

Intrathecal injection of  $75 \mu\text{g kg}^{-1}$  APO ( $n = 5$ ) led to a significant elevation ( $p < 0.05$ , Mann-Whitney *U*-test) of the t.f.l. for a period of about 12 min. In contrast, in five animals pretreated with  $10 \text{ mg kg}^{-1}$  i.v. of the D-2 antagonist sulpiride, no elevation of t.f.l. was observed following intrathecal infusion of APO. Intrathecal injection of the putative D-2 agonist LY171555 ( $75 \mu\text{g kg}^{-1}$ ) also led to a significant increase in t.f.l. ( $n = 6$ ) whereas  $150 \mu\text{g kg}^{-1}$  of the proposed D-1 agonist SK and F38393 by the same route had no effect on t.f.l. in five animals. These results suggest the involvement of a D-2 receptor mechanism in the mediation of the t.f.l.-elevating effect of APO.

Although changes in the latency of nocifensive spinal reflexes are indicative of alterations in sensory input, care must be taken when interpreting results from experiments involving drugs with a known effect on motor activity. We have therefore attempted to correlate the behavioural effects of APO on t.f.l. with changes in neuronal responses of sensory units in the dorsal horn. In this second series of experiments single-unit activity was recorded in the lumbar dorsal horn of barbiturate-anaesthetized rats using single-barrelled glass microelectrodes filled with Pontamine Sky Blue. The anterolateral surface of the contralateral cervical spinal cord was electrically stimulated to enable projection units to be identified antidromically.

The response of 12 out of 14 histologically identified dorsal horn units to noxious peripheral stimulation (pinch or heating of the hindpaw) was reversibly reduced following the i.v. injection of  $80 \mu\text{g kg}^{-1}$  APO. In contrast, the response of another ten units to low-intensity mechanical stimulation was not reduced by the same dose of APO. These results suggest that APO selectively reduces the responses of spinal sensory units to noxious but not innocuous peripheral stimulation.

The effects of APO on units projecting via the anterolateral part of the spinal cord is currently being investigated. Preliminary results have raised the possibility that dopaminergic agents may differentially affect spinal interneurons and neurons projecting centrally.

*References*

Barasi, S. & Duggal, K. N. 1984 *J. Physiol., Lond.* (In the press.)