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ABSTRACTS

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EVIDENCE TO SUGGEST A DIFFERENTIAL INVOLVEMENT OF CORTICOSTEROIDS IN THE EXPRESSION OF OPIATE AND OPIOID ANALGESIA

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Several lines of evidence now suggest that the ACTH/corticosteroid axis may be involved in the expression of opiate/opioid analgesia. Of particular relevance in this context are data indicating that adrenalectomy and corticosteroids enhance opioid/opiate analgesia[1]. Whilst these findings are strongly suggestive of a prime role for corticosteroids in the expression of opiate analgesia it is necessary to examine the influence of the absence of corticosteroids per se before firm conclusions can be drawn.

For these studies 25-30g DBA/2 mice were injected with the 11 β-hydroxylase inhibitor Metyrapone, which blocks the synthesis of corticosterone from 11-Deoxycorticosterone. In the absence of data concerning the effects of Metyrapone on baseline pain responding a series of titration studies were conducted to examine this. 30 mins following drug administration (0-160 mg/kg Metyrapone) animals were assayed for tail-flick latency (TFL) at 0,15,30,45 and 60 mins post-injection. Data were analysed by ANOVA which revealed a bi-phasic effect, with 160 mg/kg inducing significant analgesia and 1-20 mg/kg producing only weak and inconsistently reproduceable analgesia. In the second series of studies the influence of Metyrapone on analgesia induced by 5 mg/kg morphine was studied. ANOVA revealed that 20-80 mg/kg potently and 0.1-1 mg/kg partially blocked this form of antinociception. Finally, although the analgesia induced by exposure to 35 bite attacks in a standard Resident-Intruder Paradigm is known to be opioid-mediated, Metyrapone was without effect. Data from these studies are summarised below.

mg/kg Metyrapone

	0.05	0.1	0.5	1	5	10	20	40	80	160
Basal	-	-	-	*	*	*	*	-	-	***
Opioid							-	-	-	
Morphine	-	Partial Block(?)	Partial Block	Partial Block	-	-	Block	Block	Block	

- = no effect * = weak analgesia *** = potent analgesia

Current data demonstrate that Metyrapone has (i) biphasic effects on baseline pain sensitivity (ii) no influence on opioid analgesia at the doses thus far examined, yet (iii) fully blocks morphine analgesia at high and partially blocks this response at low doses. Thus, these data possibly suggest a difference in the mechanisms involved in the expression of opioid and opiate analgesia.

1. Miczek, KA et al., Annals of NY Acad Sci, 467, 14-29 (1986).