

The effect of physostigmine and neostigmine on ketamine anaesthesia and analgesia

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The anticholinesterase physostigmine has been observed to antagonize the sedative, but not the analgesic properties of the intravenous anaesthetic ketamine in humans (Balmer & Wyte, 1977). In this study the pretreatments of adult male Wistar rats (350 grams) with either physostigmine (0.3 mg/kg) or neostigmine (0.08 mg/kg) five minutes before ketamine (100 mg/kg) were compared. Groups of six animals were used, control animals received saline pretreatment and all injections were made intraperitoneally. Anaesthesia was measured as the time from the loss to the recovery of the righting reflex. The tail-immersion method (water temperature $60 \pm 1^\circ\text{C}$) was found to elicit reliable control aversion responses of 2.0 ± 0.2 s and was used as a measure of antinociceptive activity. Analgesia was said to be present when

aversion response time was 25% greater than control responses. Antinociceptive activity was calculated as the total area under the analgesia curve.

Pretreatment with the anticholinesterase agents significantly reduced ketamine anaesthesia (see Figure 1). Ketamine control showed an antinociceptive activity area of 1250 ± 520 mm². Neither anticholinesterase significantly altered this activity. Physostigmine (0.3 mg/kg) was shown to have antinociceptive activity of its own. Neostigmine (0.08 mg/kg) had no analgesic properties. There was no alteration in the duration time of the postanaesthetic analgesia in the pretreated compared to control ketamine animals.

These results confirm observations made by Balmer & Wyte (1977) that anti-cholinesterase agents can antagonize the anaesthesia without affecting the analgesia of ketamine.

D.L. is an MRC student.

Reference

BALMER, H.G.R. & WYTE, S.R. (1977). Antagonism of ketamine by physostigmine. *Br. J. Anaesth.*, **49**, 510.

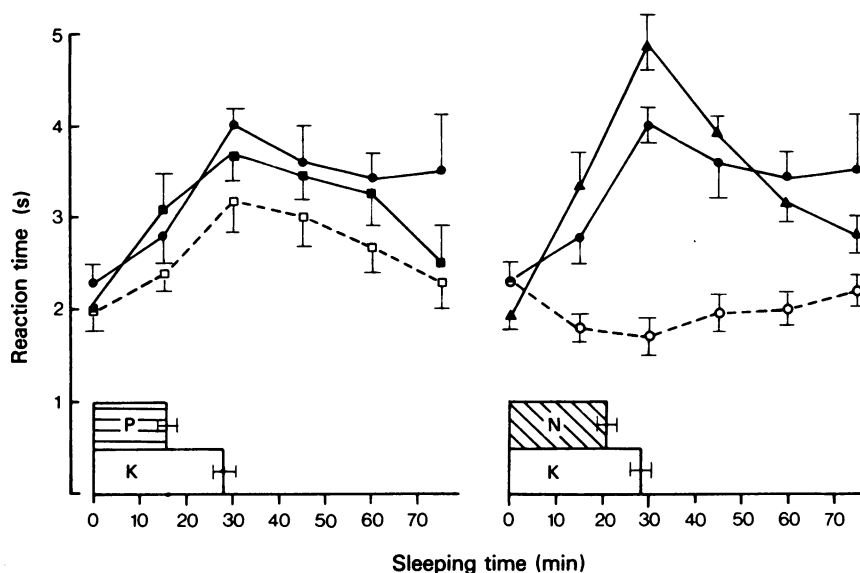


Figure 1 Graphs of time (experimental duration) against response reaction time showing the analgesic effect of ketamine (●, K), physostigmine (P) 5 minutes before ketamine (■); physostigmine alone (□); neostigmine (N) 5 minutes before ketamine (▲) and neostigmine alone (○). The sleeping time of anticholinesterase pretreatments are also shown.