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Antagonism of morphine analgesia by reserpine and α-methyltyrosine and the role played by catecholamines in morphine analgesic action

SIR,—Since Vogt (1954) showed that morphine can deplete hypothalamic noradrenaline the participation of catecholamines in the analgesic action of morphine has been proposed by many authors (Radouco-Thomas, Radouco-Thomas & Le Breton, 1957; Schaumann, 1958; Paeile & Muñoz, 1966, and others).

The effect of reserpine on the analgesic action of morphine has now been examined by means of two different tests; also, the effect of pretreatment with α-methyltyrosine on morphine analgesia was investigated. According to current views (Spector, 1966) α-methyltyrosine is a potent inhibitor of tyrosine hydroxylase which leads to a selective depletion of brain noradrenaline and dopamine without affecting 5-hydroxytryptamine.

The increase induced by morphine (5 mg/kg, i.v.) of the pain threshold when the tooth pulp of the rabbit is electrically stimulated was abolished 24 hr after the administration of reserpine (2 mg/kg, i.v.). In the same way, chronic treatment with reserpine (0·2 mg/kg, s.c., once a day, during 14 days) much reduced the

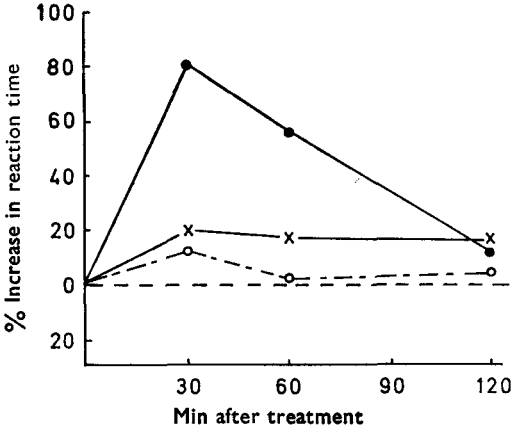

FIG. 1. Antagonism of morphine analgesic action by α-methyltyrosine in the mouse. Two doses of 100 mg/kg, i.p. of α-methyltyrosine were injected 8 and 4 hr respectively before morphine (10 mg/kg, i.p.). Analgesia was measured by the hot plate test (58° ± 0·5), according to Garcia Leme & Rocha e Silva (1961). The points on the curves represent the means of 40, 35 and 33 animals in the groups treated with morphine alone (●), morphine after α-methyltyrosine (×) or α-methyltyrosine alone (○), respectively.

analgesic response to morphine injected before the 15th dose of reserpine and abolished the analgesic response when the narcotic was tested 4 hr after that dose of the tranquillizer.

The increase produced by morphine (10 mg/kg, i.p.) in the reaction time to heat stimulation of the mouse paw (hot plate test, 58·0° ± 0·5°) was abolished 4 hr after reserpine (1 mg/kg, i.p.). The analgesic effect of morphine partially returned over a 144 hr period following reserpine treatment. On the other hand, the pretreatment with two sucessive doses of α-methyltyrosine (each of 100 mg/kg, i.p.) given 8 and 4 hr respectively before the injection of morphine nearly abolished the analgesic effect of the narcotic, measured by the hot plate test in the mouse (Fig. 1).

These results support the view that the analgesic action of morphine is mediated though liberation of brain catecholamines.

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A new nerve muscle preparation: the obturator nerve-anterior gracilis preparation of the rat

SIR,—It is well known that the rat phrenic nerve-diaphragm preparation is insensitive to certain muscle relaxant drugs (Paton & Zaimis, 1952). An alternative and possibly more sensitive preparation appears to be the obturator nerve-anterior gracilis preparation of the rat. This muscle is 1·0 mm thick (Quilliam, 1955), or about twice the thickness of the diaphragm. A good diagram of the rat anterior gracilis and obturator nerve is given by Quilliam (1955). The anterior gracilis is a strap-like muscle which arises from the pubis and is inserted into the upper end of the tibia. It is exposed by removing the skin from the thigh and removing the connective tissue. The muscle can be identified easily because the obturator nerve enters its upper border and then divides into two parallel branches which run longitudinally down the muscle towards its insertion. The obturator nerve is exposed by cutting through the pectineus muscle and is followed up to the obturator foramen. At this point the nerve can be easily sectioned and carefully separated from the underlying muscle. The origin of the anterior gracilis is exposed by removal of the pectineus muscle. The bony origin is then cut free from the pelvis with bone cutting forceps and the muscle separated from adjacent muscles. In a similar manner the insertion is separated from the rest of the tibia. The muscle and nerve are then free and can be set up in a similar manner to the phrenic nerve-diaphragm in Krebs solution, oxygenated with oxygen 95% and carbon dioxide 5% at 37°.