Changes in the responsiveness of the colon and vas deferens to nerve stimulation and injected transmitters in the pithed rat following chronic morphine treatment

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In experimental animals, chronically treated with morphine, drug withdrawal causes hyperexcitability which is probably central in origin but is partly mediated via the peripheral autonomic nervous system. There is some evidence that this hyperexcitability persists even in isolated tissues (Kaymakcalan & Temelli, 1964). This investigation sought to confirm the existence of morphine-induced hyperexcitability in peripheral autonomic neuro-effector systems and to determine if the phenomenon survived destruction of the central nervous system.

Male Wistar rats (200–300 g) were divided into three groups. One group received daily injections of morphine (4–400 mg/kg subcutaneously), supplemented by morphine in the drinking water. These rats received on average an oral dose of 2 mg/kg daily. The second (control) group received daily injections of normal saline (2 ml/kg subcutaneously). The third group was untreated.

The spinal autonomic outflows to the colon and the vas deferens were stimulated in pithed rats using the movable electrode technique (Gillespie, MacLaren & Pollock, 1969). The sensitivities of these two organs to nerve stimulation were measured. For comparison, the sensitivities of the colon to injected acetylcholine (0·01–10 mg/kg intravenously) and of the vas to injected noradrenaline (0·001–1 mg/kg intravenously) were also measured.

In saline-treated and untreated rats, acutely administered morphine (3–12 mg/kg intravenously) inhibited the responses of the colon and the vas to nerve stimulation but not to the exogenously administered transmitters. In rats chronically treated with morphine the responsiveness of the test organs to nerve stimulation depended upon the time interval between the last injection of morphine and examination. In rats examined less than 1 h after the last injection, neither the colon nor the vas responded to nerve stimulation. When examined 18 h after the last injection, the responses of the test organs to nerve stimulation were apparently similar to those of control and untreated rats. However, latent changes in the sensitivities of these organs could be revealed by acutely administered nalorphine (250 mg/kg intraperitoneally), which uncovered a marked hypersensitivity in both organs to nerve stimulation.

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Potentials in isolated rat superior cervical ganglia produced by nicotine

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Depolarization of isolated rat ganglia by acetylcholine or carbachol is followed by hyperpolarization when the drug is washed out (Pascoe, 1956; Brown, 1966). This hyperpolarization probably results from active extrusion of accumulated intra-