TABLE 1. *Cytoplasmic $^{45}Ca^{++}$ content (mmol/kg w. weight) of rat aortae immersed for 5 min± in radioactive physiological solution and during a subsequent period of 15 min. in radioactive physiological solution; in radioactive depolarizing solution or in radioactive physiological solution containing noradrenaline 10^{-5}M. Means ±S.E. of mean*

Treatment	Physiological solution	Depolarizing solution	Noradrenaline 10^{-5}M
Controls	0·055±0·002 (12)	0·088±0·004 (12)	0·089±0·004 (12)
Cinnarizine 10^{-5}M (pretreatment of 90 min.)	0·041±0·002 (12)	0·048±0·003 (12)	0·049±0·003 (12

The present results suggest that cinnarizine could act by inhibiting the opening of Ca^{++}-channels evoked by depolarization or noradrenaline and therefore by decreasing the calcium influx into the stimulated smooth muscle cell.

Supported by FRSM, grant no. 1191.

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Drug-induced changes in the sensitivity of the rat anococcygeus muscle

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Various types of supersensitivity occur in adrenergically innervated tissues. For example, specific supersensitivity to noradrenaline (NA) is produced by impairment of the neuronal uptake process, while non-specific supersensitivity occurs following decentralisation or reserpine treatment (Trendelenburg, 1966). Both these types of supersensitivity are indicated by leftwards shifts in the dose-% response curves. However, increased sensitivity may also be manifested as increases in the maximum response of the tissue to agonists (Cannon & Rosenblueth, 1949), with no shift in the dose-% response curve (Muir & Pollock, 1973). In this study the effects of various drugs on the sensitivity of the rat anococcygeus muscle (Gillespie, 1972) were investigated.

Adult male Wistar rats were stunned and killed by exsanguination. The anococcygeus muscles were removed and suspended in oxygenated Krebs bicarbonate solution (37° C). Responses to acetylcholine (ACh) and NA were recorded isometrically.

A specific supersensitivity (50–100 fold) to NA was produced by cocaine (10^{-5}M in the Krebs bathing medium) and 6-hydroxydopamine (6–OHDA) (2×50 mg/kg on day 1; 2×100 mg/kg on day 4; experiment on day 6). The responses to the α-agonist, oxymetazoline, which is not taken up by the nerves (Birmingham, Paterson & Wojcicki, 1970), were unaffected by these drugs, suggesting that the specific supersensitivity following cocaine and 6–OHDA resulted from impaired neuronal uptake. Reserpine (1[mg/kg]/day; 6 days) produced a 2-fold increase in sensitivity to both ACH and NA. Thyroxine (3[mg/kg]/day orally in drinking water for 2 weeks) had a similar effect. In neither of these types of supersensitivity, which were characterized by displacement of the dose-% response curves, was the maximum response to either agonist altered. Corticosterone (10[mg/kg]/day; 6 days) produced a third type of supersensitivity, similar to that produced by morphine withdrawal in other tissues (Pollock, Muir, MacDonald & Henderson, 1972) and characterized by an increase in the maximum to both agonists. In this study of morphine (300[mg/kg]/day orally in drinking water for 4 months) produced a similar pattern of supersensitivity to that produced by corticosterone.

Thus, at least three types of supersensitivity occur in the rat anococcygeus. The mechanism of the specific supersensitivity seems clear but the different types of non-specific supersensitivity produced by reserpine and thyroxine on the one hand and corticosterone and morphine on the other are unexplained and require further examination.

The gift of oxymetazoline from Dr. D. Jack of Allen and Hanburys and the financial assistance of the Rankin Fund are gratefully acknowledged.
A. G. is an M.R.C. Scholar.

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The effect of electrical stimulation of the myenteric plexus-longitudinal muscle preparation of the guinea-pig ileum on its acetylcholine content

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The acetylcholine (ACh) content of the myenteric plexus-longitudinal muscle preparation was determined after extraction with trichloroacetic acid (Chang & Gaddum, 1933) by bioassay on the isolated guinea-pig ileum (Kosterlitz, Lydon & Watt, 1970). When such a preparation was incubated in Krebs solution containing choline (20 μM), the ACh content rose over a period of 30 min and was then maintained at a steady level for at least 240 min. In the presence of eserine (7·7 μM) the rate of rise was greater, the ACh content continued to increase slightly after 30 min and the final content was approximately double that in the absence of eserine.

After incubation for 70 min in the presence or absence of eserine, the tissue was homogenized in ice-cold 0·32 M sucrose solution containing eserine by means of a Teflon pestle—glass homogenizer and subsequently fractionated by differential centrifugation into nuclear (600 *g*, 20 min), mitochondrial (22,000 *g*, 30 min), microsomal (100,000 *g*, 60 min) and supernatant fractions. Comparisons of the fractions prepared from tissues incubated in the presence or absence of eserine showed that there was little difference between the ACh contents of the particulate fractions. In the supernatant fraction, however, eserine increased the ACh content by an average of 12 μg/g tissue, most of which was not protein-bound.

In a second series of experiments, preparations were pre-incubated for 70 min in the presence of eserine and then incubated for a further 60 min in the same solution either without stimulation or with supramaximal stimulation (1 ms pulse duration), at 0·017, 1 or 10 Hz. The ACh contents of the stimulated and unstimulated preparations were compared with the contents of tissues incubated for only 70 min. The spontaneous as well as the stimulated ACh outputs occurring during the second or main incubation period of 60 min were measured and the rate of synthesis of ACh determined. As far as ACh content is concerned there was no significant change at the lower frequencies but a decrease of 30% at 10 Hz. This decrease was nearly all accounted for by the ACh released during stimulation so that there appeared to be no synthesis of ACh during this period. Fractionation of the tissue showed that the decrease in the ACh content stimulation was due mainly to loss from the supernatant fraction.