

by guanethidine. As the electrode was moved upwards towards the cervical region, stimulation increasingly affected the heart rate and the blood pressure, both of which dramatically increased. Adrenalectomy reduced this response and abolished the secondary pressor effect, which increased for some time after stimulation ceased. Stimulation in the upper thoraco-lumbar region caused an immediate cardio-accelerator effect without affecting the blood pressure.

REFERENCE

- GILLESPIE, J. S. & MUIR, T. C. (1967). A method of stimulating the complete sympathetic outflow from the spinal cord to the blood vessels in the pithed rat. *Br. J. Pharmac. Chemother.*, **30**, 78-87.

The effect of decentralization and reserpine-treatment on the sensitivity of the isolated vas deferens of the guinea-pig to stimulant drugs

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The non-specific, time-dependent supersensitivity to drug stimulation which is observed *in vivo* in smooth and cardiac muscle following decentralization or treatment with reserpine is not always seen *in vitro* (Tsai *et al.*, 1968; Westfall & Fleming, 1968). The purpose of the current investigation was to determine whether such supersensitivity could be demonstrated *in vitro* in the smooth muscle of the vas deferens.

Desheathed vasa deferentia from guinea-pigs were suspended in organ baths in Krebs solution at 37° C. Contractions in response to drugs were recorded with strain gauges. The tissues were obtained from guinea-pigs which received (1) no treatment (control), (2) reserpine-treatment for either 1 or 5 days (1.0 mg/kg per

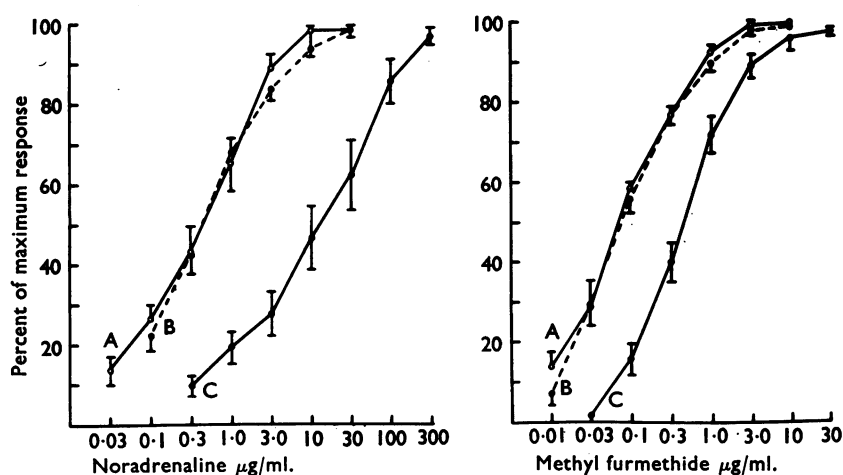


FIG. 1. Mean dose-response curves to noradrenaline and methyl furmethide in isolated vasa deferentia from guinea-pigs receiving no treatment ($N=15$), 5 days of reserpine ($N=10$) or 5 days after decentralization of the vas deferens ($N=8$). Abscissa, dose of agonist expressed as $\mu\text{g/ml}$ of bath solution; ordinate, amount of contraction expressed as % of the maximum contraction. A, reserpine (5 days); B, decentralized (5 days). C, control.

day), or from (3) animals in which 1–2 cm of both hypogastric nerves were removed 1 or 5 days previously.

One day treatment failed to cause supersensitivity. Both 5-day reserpinization and 5-day decentralization resulted in a substantial increase in sensitivity to nor-adrenaline and methyl furmethide (Fig. 1). Similar results were obtained when histamine and potassium were used as stimulants, although the magnitude of the sensitivity increase to potassium (1.5-fold at the ED₅₀) was considerably less than that to the other agents.

Fleming (1963) proposed, on the basis of indirect evidence, that an alteration of the electrical properties of the smooth muscle cell membrane might be involved in the development of supersensitivity. Since the vas deferens exhibits supersensitivity *in vitro*, as shown by the present experiments, a study of the electrophysiological behaviour and of the ion distribution in this tissue is now in progress.

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REFERENCES

- FLEMING, W. W. (1963). Changes in the sensitivity of the cat's nictitating membrane to norepinephrine, acetylcholine and potassium. *Biochem. Pharmac.*, **12**, suppl. 262.
- TSAI, T. H., DENHAM, S. & MCGATH, W. R. (1968). Sensitivity of the isolated nictitating membrane of the cat to norepinephrine and acetylcholine after various procedures and agents. *J. Pharmac. exp. Ther.*, **164**, 146–157.
- WESTFALL, D. P. & FLEMING, W. W. (1968). The sensitivity of the guinea-pig pacemaker to norepinephrine and calcium after pretreatment with reserpine. *J. Pharmac. exp. Ther.*, **164**, 259–269.

The inhibitory innervation of the bovine iris sphincter

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The presence of an inhibitory, as well as an excitatory, component in the innervation of the sphincter pupillae has been known for some years (Joseph, 1921). Anatomical evidence for adrenergic innervation to the sphincter is well documented for a number of species (Laties & Jacobovitz, 1966; Malmfors, 1965; Richardson, 1964). In this work the nature of the adrenergic innervation of the bovine iris sphincter has been further investigated. Isolated preparations of sphincter muscle were used to study the effects of transmural electrical stimulation and of directly acting sympathomimetics and the modification of these effects by blocking agents.

Eyes were removed from cows immediately after killing, and stored in Krebs solution at 3°–4° C until used (2–24 hr). Iris sphincter loops were dissected from the eyes and mounted in Krebs at 37° C aerated with 95% O₂/5% CO₂. Movements of the sphincter were recorded isotonically under a tension of 450 mg. Preparations were stimulated transmurally from a square wave stimulator. The parameters of stimulation were 150 V, 0.3 msec pulse width and frequencies of 2 to 80/sec for periods of 15 sec at intervals of 5.5 min.

Recordings were begun when the tissue had taken up a steady spontaneous level of tone (usually after about 2 hr). The sphincter then gave a biphasic response to transmural stimulation, the contractile phase of which could be abolished, at all frequencies used, by hyoscine (5×10^{-8} g/ml.). Eserine or neostigmine potentiated this component in concentrations of 10^{-6} g/ml. The α -receptor blocking agents phentolamine or piperoxan in concentrations up to 10^{-5} M had no significant inhibitory