REFERENCES

AXELROD, J. (1954). *J. Pharmac. exp. Ther.*, **110**, 315–325.
DAVIS, V. E., BROWN, H., HUFF, J. A. & CASHAW, J. L. (1967). *J. Lab. clin. Med.*, **69**, 132–140.
DAVIS, V. E., BROWN, H., HUFF, J. A. & CASHAW, J. L. (1967a). *Ibid.*, **69**, 787–799.
DRING, L. G., SMITH, R. L. & WILLIAMS, R. T. (1966). *J. Pharm. Pharmac.*, **18**, 402–405.
TACKER, M., CREAVEN, P. J. & MCISAAC, W. M. (1969). *Biochem. Pharmac.*, in the press.

Observations on some actions of ergometrine, noradrenaline and dopamine on the guinea-pig vas deferens and on the rabbit jejunum

Some of the effects of dopamine may be brought about by an action on specific dopamine receptors as opposed to an action on α- or β-adrenergic receptors (McDonald & Goldberg, 1964; Eble, 1964; Rossum, 1965, 1966; Goldberg, Sonneville & McNay, 1968; Woodruff & Walker, 1969). In the brain of the snail, *Helix aspersa*, dopamine hyperpolarizes and inhibits some of the neurons by an action on specific dopamine receptors (Woodruff & Walker, 1969) and this action of dopamine is blocked by low concentrations of ergometrine, less effectively by α-blocking agents (Walker, Woodruff & others, 1968). Ergometrine has little or no α-blocking activity (Brown & Dale, 1935).

Cumulative concentration–effect curves were obtained for dopamine and for (—)-noradrenaline on the guinea-pig vas deferens, using the method of Rossum (1963). The mean pD_2 values were 4·6 for dopamine, and 5·6 for noradrenaline. Ergometrine maleate 10^{-6} to 5×10^{-6} M potentiated the response to noradrenaline (Fig. 1A), taking the form of an increase in the maximum effect obtainable, which rose to between 120% and 200% of control values. In Fig. 1A, there is also seen a shift to the left of the concentration–effect curve, but in other experiments in which ergometrine produced either no shift of the concentration–effect curve or a slight shift to the right, there was still seen an increase in the maximum response to noradrenaline. This action of ergometrine was reversed on washing. In contrast to its action on the noradrenaline response, ergometrine 2×10^{-6} to 10^{-5} M caused a decrease in the maximum effect of dopamine on the vas deferens. Over the lower concentration ranges of dopamine ergometrine caused potentiation of the response. Ergometrine alone had no effect on the vas deferens in concentrations up to 10^{-4} M.

Concentration–effect curves were obtained also on the isolated rabbit jejunum, using the method described by Rossum (1965). The mean pD_2 values obtained were 4·8 for dopamine and 7·0 for noradrenaline. In the presence of an amount of ergometrine (2×10^{-6} M), which itself had no effect on rhythmic activity, noradrenaline in concentrations of from 3×10^{-8} M to 10^{-6} M caused an increase in the amplitude of the spontaneous contractions instead of the usual decrease (Fig. 1B). Higher concentrations of noradrenaline in the presence of ergometrine caused the usual inhibition, with a small shift to the right of the concentration–effect curve, but with no change in the maximum effect obtainable (Fig. 1B). Similar results were obtained with dopamine as the agonist, with which ergometrine was less effective in reversing the inhibitory action of low concentrations, but caused a greater shift to the right of the concentration–effect curve. Ergometrine in concentrations greater than 10^{-5} M had a variable, but generally inhibitory, action on rhythmic activity.

One possible explanation of our observation on the rabbit jejunum is that ergometrine uncovers an excitatory action of noradrenaline, mediated through different receptors, perhaps also sympathomimetic. The mechanism of action of ergometrine on the vas deferens could possibly be similar to that suggested by Barnett, Greenhouse & Taber (1968) for other compounds on the rat vas deferens.

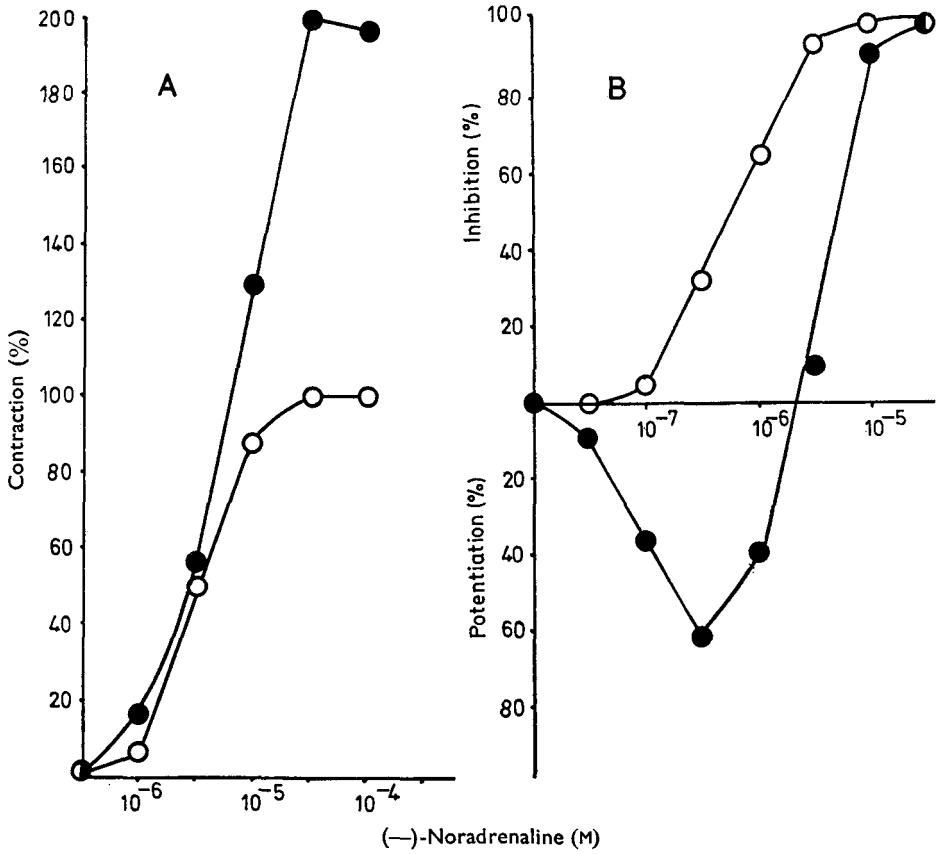

FIG. 1A. Cumulative concentration–effect curves for (−)-noradrenaline on the isolated guinea-pig vas deferens. ○—○ control curve. In the presence of 2×10^{-6} M ergometrine maleate, ●—●, there was a large increase in the maximum response.

B. Concentration–effect curves for (−)-noradrenaline on the isolated rabbit jejunum. ○—○ control curve. In the presence of 2×10^{-6}M ergometrine maleate, ●—●, there was a reversal of the effect of low concentrations of noradrenaline.

Department of Physiology and Biochemistry,
The University,
Southampton, England.
July 31, 1969

G. N. WOODRUFF
J. AGAR
M. J. ALBANI
K. A. ALLEN
J. FOLKARD

REFERENCES

BARNETT, A., GREENHOUSE, D. D. & TABER, R. I. (1968). *Br. J. Pharmac.*, **33**, 171–176.
BROWN, G. L. & DALE, H. (1935). *Proc. R. Soc. B.*, **118**, 446–477.
EBLE, J. N. (1964). *J. Pharmac. exp. Ther.*, **145**, 64–70.
GOLDBERG, L. I., SONNEVILLE, P. F. & MCNAY, J. L. (1968). *Ibid.*, **163**, 188–197.
MCDONALD, R. H. & GOLDBERG, L. I. (1963). *J. Pharmac. exp. Ther.*, **140**, 60–66.
ROSSUM, J. M. VAN (1963). *Archs int. Pharmacodyn. Thér.*, **143**, 299–330.
ROSSUM, J. M. VAN (1965). *J. Pharm. Pharmac.*, **17**, 202–216.
ROSSUM, J. M. VAN (1966). *Archs int. Pharmacodyn. Thér.*, **160**, 492–494.
WALKER, R. J., WOODRUFF, G. N., GLAIZNER, B., SEDDEN, C. B. & KERKUT, G. A. (1968). *Comp. Biochem. Physiol.*, **24**, 455–469.
WOODRUFF, G. N. & WALKER, R. J. (1969). *Int. J. Neuropharmac.* **8**, 279–289.