HUGHES, J. (1972). Evaluation of mechanisms controlling the release and inactiveness of the adrenergic transmitter in the rabbit portal vein and vas deferens. *Br. J. Pharmac.*, **44**, 472.

MARSHALL, I., NASMYTH, P.A. & SHEPPERSON, N.B. (1977). Presynaptic α-adrenoceptors and [^{3}H]-noradrenaline overflow from the mouse vas deferens. *Br. J. Pharmac.* (This meeting).

SEVER, P., OSIKOWSKA, B., BIRCH, M. & TUNBRIDGE, R.D.G. (1977). Plasma noradrenaline in essential hypertension. *Lancet*, 1, 1078–1081.

STJÄRNE, L. (1975). Clonidine enhances the secretion of sympethetic neurotransmitter from isolated guinea-pig tissues. *Acta Physiol. Scand.*, **83**, 142–144.

Presynaptic inhibition of acetylcholine release from cholinergic neurones in the myenteric plexus of the guinea-pig ileum

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The isolated ileum of the guinea-pig suspended in Krebs solution releases acetylcholine (ACh) spontaneously into the surrounding fluid. This ACh has its origin in the intramural nerve plexus (Johnson, 1963; Paton & Zar, 1968). Johnson (1963) found that when the ACh from such ileal segments was collected during 5, 10, 20, or 40 min periods the total amount recovered increased with the increasing collection time, but the rate of spontaneous release fell progressively.

The possibility arises that the accumulation of ACh in the synaptic cleft inhibits the further output of the transmitter and in support of this suggestion Kilbinger & Wagner (1975) showed that oxotremorine caused an atropine sensitive reduction in spontaneous output of ACh from guinea-pig ileum treated with physostigmine or DFP. Kilbinger & Wagner also postulated that oxotremorine acted on a neuronal receptor responsible for feedback control of ACh release from the ileum at rest.

A different observation, this time on the electrically transmurally stimulated guinea-pig ileum, seems relevant. When the ileum was contracted submaximally by a train of stimuli (0.2 Hz) until constant responses were obtained, and then with the current off a dose of ACh was added for 30 s and then washed out, electrical restimulation at this point resulted in smaller twitches than those obtained before the ACh. Recovery of the twitch responses after ACh to control height took 8–10 minutes. ACh caused a dose-dependent inhibition of the twitch response to electrical stimulation over the concentration range 0.85 nM-68.4 μM.

The increase in efflux of [^{3}H]-ACh on electrical field stimulation of ileal strips pretreated with 99 μM [^{3}H]-choline for 2 h, was inhibited by exogenous ACh (1.7 μM) in Krebs containing physostigmine (0.18 μM) and hemicholinium (17 μM). This inhibition of [^{3}H]-ACh efflux was reversed by atropine (0.35 μM).

These experiments appear to provide direct evidence that exogenous ACh can inhibit the output of transmitter ACh by an action on a presynaptic muscarinic cholinoceptive receptor.

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References

JOHNSON, E.S. (1963). The origin of the acetylcholine released spontaneously from the guinea-pig isolated ileum. *Br. J. Pharmac.*, **21**, 555–568.

KILBINGER, H. & WAGNER, P. (1975). Inhibition by oxotremorine of acetylcholine resting release from guinea-pig ileum longtitudinal muscle strips. *Naunyn-Schmiedeberg's Arch. Pharmac.*, **287**, 47–60.

PATON, W.D.M. & ZAR, M.A. (1968). The origin of acetylcholine released from guinea-pig intestine and longtitudinal muscle strips. *J. Physiol., Lond.*, **194**, 13–33.