haloperidol, did not alter the effect of bromocriptine ($n = 7$).

A cholinoceptive or β-adrenoceptive origin of the increase in flow by bromocriptine was excluded since atropine and propranolol, given in doses that completely blocked the responses to, respectively, acetylcholine and isoprenaline, had no influence on the responses to bromocriptine ($n = 3$). The possibility that bromocriptine increases femoral flow through a partial agonism at postsynaptic α-adrenoceptors is unlikely since even 8×10^{-8} mol bromocriptine injected into the denervated hindlimb did not influence the vasoconstriction produced by locally injected noradrenaline ($n = 5$).

The present experiments suggest that bromocriptine, besides its stimulating effect on postsynaptic α-adrenoceptors, increases femoral flow through stimulation of dopamine receptors presumably located on sympathetic nerve endings, as described for apomorphine (Buylaert *et al.*, 1977). The duration of action of bromocriptine is much longer than with apomorphine as also seen for central dopamine receptors (Corrodi, Fuxe, Hökfelt, Lidbrink & Ungerstedt, 1973).

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Disposition of adrenergic neurotransmitter in saphenous veins of dog and rabbit

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In an earlier paper we reported a difference in sensitivity of saphenous vein segments of dog and rabbit to exogenous noradrenaline, which disappeared after blockade of neuronal uptake by cocaine. No differences between the two species were noted as regards the shape of the frequency-response curve to nerve stimulation (De Mey & Vanhoutte, 1977). The present study was designed to compare, in veins from both animals, the pattern of metabolism of the adrenergic transmitter in basal conditions and during sympathetic nerve activity.

Saphenous veins of dogs and rabbits first were incubated in Krebs–Ringer solution containing 7-[^{3}H]-noradrenaline (3×10^{-7} M; [^{3}H]-NA); they were then mounted for superfusion as previously described (Vanhoutte, Lorenz & Tyce, 1973). The superfusate was collected at given intervals for estimation of total radioactivity ([^{3}H]-efflux) and column chromatographic separation of intact [^{3}H]-NA and its major metabolites (3,4-dihydroxymandelic acid, DOMA; 3,4-dihydroxyphenylglycol, DOPEG; 3-methoxy-4-hydroxyphenylglycol, MOPEG; normentanephrine, NMN; and 3-methoxy-4-hydroxymandelic acid, VMA), as previously described (Verbeuren, Coen & Vanhoutte, 1977).

In basal conditions, the total [^{3}H]-efflux, expressed as d/min per mg wet weight, was significantly greater for veins of the dog than for those of the rabbit. In the dog, the amounts of intact [^{3}H]-NA, and of VMA present in the superfusate were significantly larger than for the rabbit; in the latter, DOPEG and DOMA constituted a significantly larger fraction of the [^{3}H]-efflux than in the dog and MOPEG was the only important O-methylated-deaminated metabolite. In the rabbit the ratio of intact [^{3}H]-NA to the total metabolite fraction was significantly smaller than in the dog.

Electrical stimulation (2 Hz) caused an increase in total [^{3}H]-efflux, which was significantly larger for dogs' veins. This increase consisted mainly of intact [^{3}H]-NA for the dog (56.2 ± 5.4 and $33.8 \pm 5.7\%$ of the total increase in [^{3}H]-efflux for dog and rabbit respectively), and mainly of MOPEG for the rabbit (33.1 ± 1.5 and $42.8 \pm 3.0\%$ for dog and rabbit respectively). As regards the other metabolite fractions, NMN contributed to the increase in [^{3}H]-efflux significantly more in the dog than in the rabbit; the VMA fraction significantly increased in the rabbit and, significantly decreased in the dog veins during electrical stimulation. The changes in the appearance of DOPEG and DOMA with electrical stimulation were comparable in both species.

These results suggest that (a) under basal conditions, intraneuronal leakage of the transmitter and subsequent deamination to DOPEG is more important in rabbit than in dog saphenous veins, (b) the

transmitter released during nerve activity is more intensely metabolised in the rabbit saphenous veins, probably because the synaptic cleft is smaller than in the dog veins, (c) at the smooth muscle level the metabolism of the adrenergic transmitter may be different, since in rabbit veins most of the NMN is quickly degraded to MOPEG whereas dog veins produce substantial amounts of intact NMN and VMA, (d) these differences in the metabolism of the adrenergic transmitter cannot be explained in terms of a difference in the density of the adrenergic innervation.

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Effects of clonidine and noradrenaline on the release of [^{3}H]-noradrenaline from the rat anococcygeus

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Rat isolated anococcygeus can accumulate [^{3}H]-noradrenaline ([^{3}H]-NA) in the adrenergic nerve terminals (Nash, Gillespie & Robertson, 1974), and is a suitable preparation for studying mechanisms involved in the release of NA (McGrath & Olverman, 1977).

Individual anococcygii were incubated in Krebs solution containing (±)-7-[^{3}H]-NA (0.5 μM; 5 μCi/ml) and ascorbic acid (20 μg/ml) at 37°C for 30 minutes. At the end of the incubation period, the tissue was washed repeatedly with Krebs solution containing nortriptyline (30 nM) for 90 min and then suspended in a 2.5 ml organ bath between two parallel platinum electrodes and superfused with Krebs solution (0.33 ml/min) containing nortriptyline (30 nM). After 30 min of equilibration, seven sequential 5 ml samples of superfusate (each corresponding to a 15-min period) were collected for total radioactivity count. Electrical field stimulation (1 ms pulses at 10 Hz) was delivered during the fourth collection period and consisted of either short trains (trains of 5 pulses, once every 30 s, for 15 min) or a single long train of 150 pulses. At the end of the experiment, the tissue was solubilized and total radioactivity counted using Intertechnique liquid scintillation spectrometer (ABAC SL 40).

Electrical field stimulation resulted in an increase in the basal efflux of tritium; the increase was calcium dependent and tetrodotoxin-sensitive. Unlabelled NA caused a rise in the basal tritium efflux; the effect was slight with NA (0.1 μM) but massive with NA (10 μM). Stimulation-induced tritium efflux remained unaffected by NA (0.1 μM) but was lost after NA (10 μM). Pretreatment with phentolamine (5 μM) did not antagonize the effects of NA on tritium efflux.

Clonidine (1–10 nM) inhibited the increase in tritium efflux evoked by short trains of electrical stimulation but exerted no effect on the basal efflux itself. Its action was blocked completely by phentolamine (5 μM) which itself potentiated the stimulation-induced tritium efflux. Clonidine was totally ineffective in inhibiting the tritium efflux evoked by long trains of electrical stimulation.

These results confirm the earlier conclusions, obtained indirectly (Idowu & Zar, 1976), that clonidine inhibits the motor transmission in the anococcygeus through presynaptic mechanisms and is effective only at short train-lengths of electrical stimulation.

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