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An electrophysiological study of presynaptic α-adrenoceptors in the vas deferens of the mouse

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1 Effects of clonidine and α-adrenoceptor antagonists were studied on sympathetic neuroeffector transmission in the mouse vas deferens. The amplitude of excitatory junction potentials (e.j.ps) was taken as a measure of transmitter release per impulse.

2 At a concentration of 0.5 μM, prazosin abolished depolarizations evoked by iontophoretically applied noradrenaline, but changed neither spontaneous nor nerve stimulation-evoked e.j.ps.

3 Yohimbine 0.1 and 1 μM, rauwolscine 1 μM and corynanthine 1 μM did not change the e.j.p. amplitudes elicited by the first 2–3 pulses in trains of 15 pulses at 3 Hz, but increased the e.j.ps elicited by the subsequent pulses. Corynanthine 1 μM was much less effective than yohimbine 1 μM or rauwolscine 1 μM, and corynanthine 0.1 μM had no effect.

4 Clonidine 0.01 μM reduced the e.j.p. amplitudes evoked by single pulses and its effect was counteracted by yohimbine 1 μM.

5 In vasa deferentia from reserpine-treated mice the e.j.p. trains were changed in much the same way as by yohimbine and rauwolscine. Yohimbine 1 μM did not further increase the e.j.p. amplitudes in these organs, whereas clonidine 0.01 μM caused a marked inhibition.

6 It is concluded that the release of the motor transmitter in the mouse vas deferens is inhibited by activation of presynaptic α-adrenoceptors, and that these receptors are normally activated by neurally released noradrenaline.

Introduction

The motor transmitter of the postganglionic sympathetic neurones of the mouse vas deferens is noradrenaline (Farnebo & Malmfors, 1971; Henderson, Hughes & Kosterlitz, 1972; Bennett & Middleton, 1975a; Jones & Spriggs, 1975), although some of the receptors for the transmitter at the smooth muscle cells may differ from α- and β-adrenoceptors, and the contribution of a second, unknown motor transmitter has not been entirely ruled out (Jenkins, Marshall & Nasmyth, 1977; Marshall, Nasmyth & Shepperson, 1978b). As in many other noradrenergically innervated tissues, the release of the motor transmitter is inhibited by activation of presynaptic α-adrenoceptors. This has been shown in experiments in which either the contractions of the tissue (Marshall, Nasmyth, Nicholl & Shepperson, 1978a) or the overflow of tritiated noradrenaline (Baker & Marshall, 1982) was taken to indicate transmitter release. Judging from the effects of subtype-selective drugs such as clonidine and yohimbine (see Starke, 1981), the presynaptic receptors are of the α_2-type (Marshall *et al.*, 1978a; Baker & Marshall, 1982).

The amplitude of excitatory junction potentials (e.j.ps) recorded from single smooth muscle cells of the mouse vas deferens is a measure of transmitter release per impulse. Thus, it should be possible to demonstrate presynaptic α-receptors also by this electrophysiological method. In fact, α-adrenoceptor antagonists reversed the normal depression in e.j.p. amplitudes at frequencies higher than 1 Hz to facilitation, and these results were interpreted in terms of the blockade of presynaptic α-receptors (Bennett, 1973; Bennett & Middleton, 1975b). However, very high concentrations of non-selective antagonists were used in those experiments. We have now investigated in the same organ, effects on e.j.p. amplitudes of low concentrations of compounds with selectivity for α_2- or α_1-adrenoceptors (see Starke, 1981). Changes in e.j.p. amplitudes produced by reserpine (Bennett & Middleton, 1975a) have also been explained on the basis of the presynaptic α-receptor concept (Starke, 1977). Therefore, we examined in addition the action of clonidine and yohimbine on vasa deferentia from reserpine-treated mice.

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While this work was in progress, Blakeley, Cunnane & Petersen (1981) published an electropharmacological analysis of the effects of some compounds with α-adrenoceptor affinity in the vas deferens of the guinea-pig. Most of our results agree well with those of these authors.

Methods

Recording of e.j.ps

Male NMRI mice (30–40 g) were decapitated. The vasa deferentia were stripped of their mesenteric sheaths. The prostatic portion of the organ (approx. 1 cm) was pinned to the bottom of a perspex organ bath with a volume of approximately 1.5 ml, and was continuously superfused at a rate of 1 ml/min with Krebs solution. The solution contained (mM): NaCl 118, KCl 4.8, $CaCl_2$ 2.5, $MgSO_4$ 1.2, KH_2PO_4 0.9, $NaHCO_3$ 25 and glucose 11; it was bubbled with 5% CO_2 in O_2 and warmed to 37°C.

The intramural nerves were stimulated with bipolar platinum electrodes placed perpendicularly to the length of the organ at its prostatic end and about 1 mm apart. Trains of 15 pulses of 1 ms duration each and a frequency of 3 Hz were used for stimulation. The voltage was adjusted so that the amplitude of the first e.j.p. in a train was approximately 10 mV. After two trains of 15 pulses, train interval 3 min, the drug under study was added, and 8 min later two further trains of 15 pulses were administered. The e.j.p. amplitudes of the two corresponding trains were averaged. In some experiments, single stimuli of 1 ms duration and of sufficient intensity to give an e.j.p. of about 25 mV were used. Successive stimuli were separated by intervals of 30 s. In each vas deferens, all e.j.ps were recorded from a single cell. If the cell was lost too early, the experiment was discarded. E.j.ps were recorded about 1 mm from the nearest stimulating electrode, as described previously (Illes & Schulz, 1980; Illes, Zieglgänsberger & Herz, 1980). Glass microelectrodes filled with 2.5 M KCl and having tip resistances of 50–70 MΩ were used.

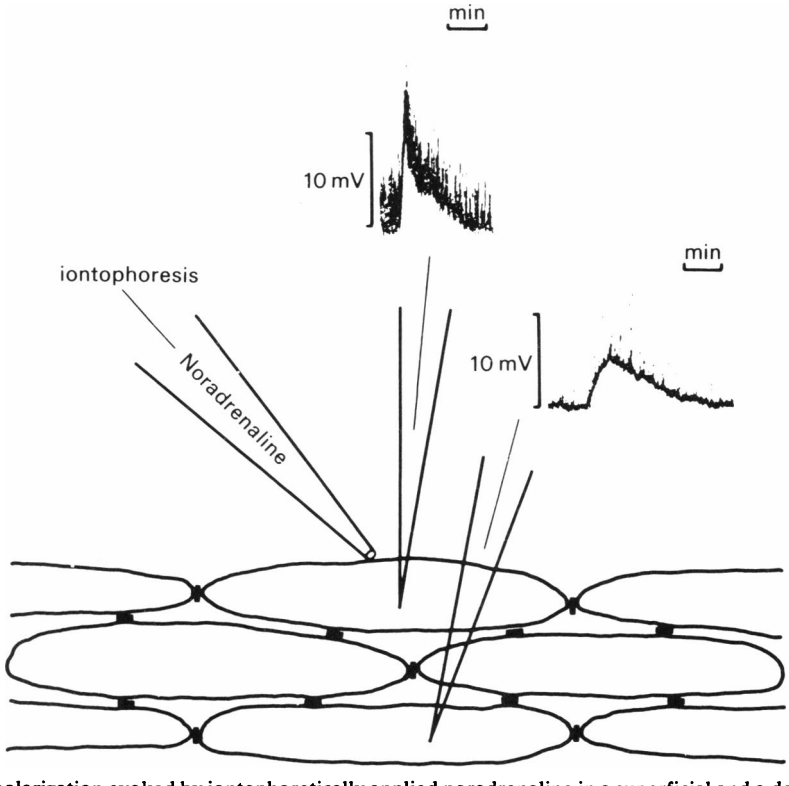

Figure 1 Depolarization evoked by iontophoretically applied noradrenaline in a superficial and a deep muscle cell of the mouse vas deferens. Noradrenaline was ejected for 3 s periods at a current strength of 20 nA (superficial cell) or 300 nA (deep cell). Note the much higher frequency of spontaneous e.j.ps and the faster time course of the response to noradrenaline in the superficial cell. The black dots connecting the smooth muscle cells represent low resistance pathways.

Noradrenaline iontophoresis

Pieces of the vas deferens, 5 mm in length, were split open longitudinally and pinned under slight tension with the inside down onto the bottom of a perspex bath. A single cell was impaled with a glass microelectrode for registration of the membrane potential as described above. A second glass microelectrode, tip size about 2 μm and filled with noradrenaline bitartrate solution 0.1 M (pH 4), was positioned close to the recording electrode (intertip distance < 5 μm). A retaining current of 10–15 nA was applied. When ejection currents were switched on for periods of less than 0.5 s, no depolarization could be observed. Therefore, ejection currents for noradrenaline were routinely applied for 2–3 s.

The superficial muscle cells of the mouse vas deferens usually have a low membrane potential (< 65 mV), high input resistance (> 30 MΩ) and high frequency of spontaneous e.j.ps, whereas the deep muscle cells are usually characterized by relatively high membrane potential (> 65 mV), low input resistance (<30 MΩ) and a low frequency of spontaneous e.j.ps (Figure 1; see also Holman, Taylor & Tomita, 1977). We used the superficial cells for iontophoresis because they responded to low iontophoretic currents with rapid depolarizations. Deep cells responded only to high iontophoretic currents with slow depolarizations (Figure 1). The reason may be that the deep cells are not depolarized directly by the ejected noradrenaline, but by a decremental conduction of the primary depolarization elicited in the superficial cells.

Depletion of tissue noradrenaline

NMRI mice were pretreated with reserpine 5 mg/kg subcutaneously 48 h and 2.5 mg/kg intraperitoneally 24 h before they were killed. Some animals received in addition (±)-α-methyl-*p*-tyrosine methylester HCl (200 mg/kg i.p.) 4, 2 and 1 h before they were killed. When this schedule is used tissue noradrenaline is depleted by 96.5% with reserpine alone, and by 99.4% when reserpine and α-methyl-*p*-tyrosine are combined (Marshall *et al.*, 1978b).

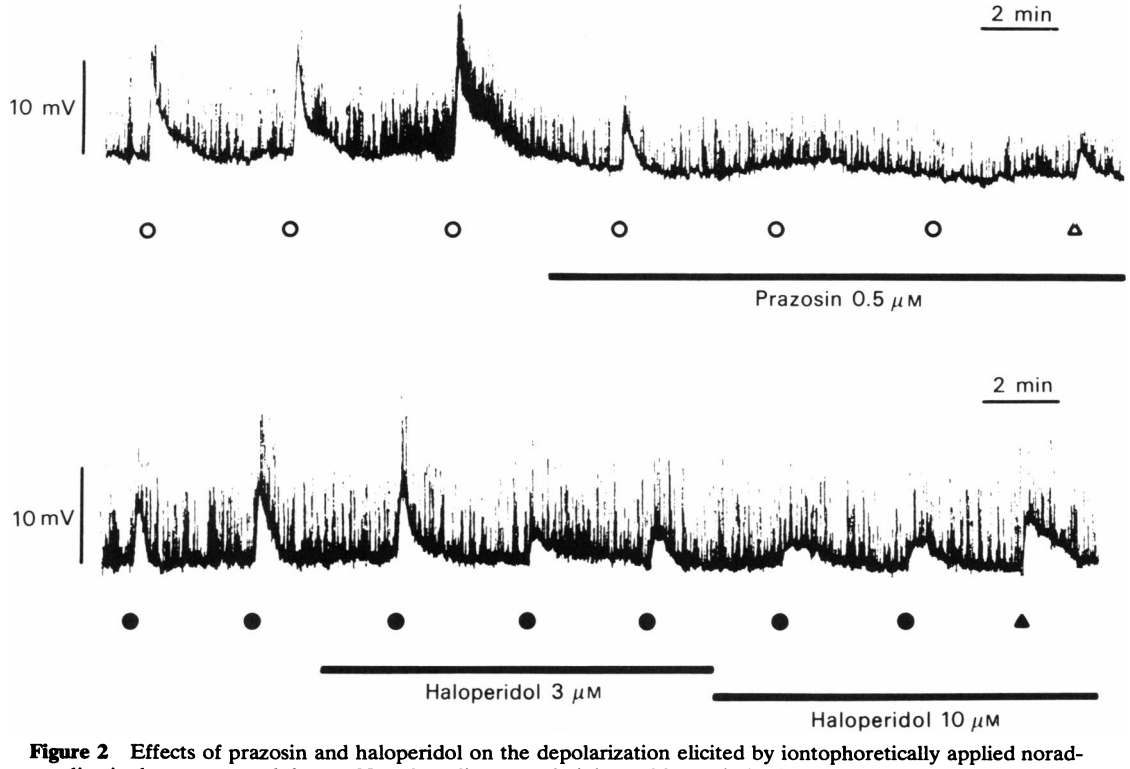

Figure 2 Effects of prazosin and haloperidol on the depolarization elicited by iontophoretically applied noradrenaline in the mouse vas deferens. Noradrenaline was administered for periods of 3 s each at ejection currents of 20 (○), 400 (△), 30 (●) and 150 nA (▲). Prazosin and haloperidol were added to the superfusion medium as indicated. Typical tracing from 3 (prazosin) or 4 (haloperidol) experiments.

Drugs and statistics

Drugs used were: clonidine HCl (Boehringer, Ingelheim), reserpine (Serpasil ampuls 0.25%, Ciba-Geigy, Basel), (±)-α-methyl-*p*-tyrosine methylester HCl (Labkemi, Göteborg), prazosin HCl (Pfizer, Karlsruhe), corynanthine HCl, rauwolscine HCl (Roth, Karlsruhe) and (−)-noradrenaline bitartrate (Sigma, München).

Means ± s.e. are given throughout. Differences between means were tested for statistical significance by Student's *t* test.

Results

Iontophoretic responses to noradrenaline

Iontophoretically applied noradrenaline reproducibly depolarized the superficial muscle cells of the mouse vas deferens (Figure 2). Prazosin 0.5 μM abolished noradrenaline-evoked depolarizations without affecting the spontaneous e.j.ps. An increase in iontophoretic current partly restored the response to noradrenaline. Haloperidol even at high concentrations (3 and 10 μM) depressed the effect of noradrenaline only moderately (Figure 2). Phentolamine 1 μM acted like prazosin 0.5 μM (not shown).

Effects of α-adrenoceptor antagonists on e.j.p. amplitudes

Electrical stimulation of the intramural nerves with trains of 15 pulses at 3 Hz elicited e.j.ps which were subject to facilitation. A typical example is shown in the inset of Figure 3. In the absence of drugs, the e.j.ps elicited by successive trains were well reproducible, as shown by the control experiments of Figure 4, and their further statistical evaluation in Table 1.

At the same concentration (0.5 μM) that abolished the response to exogenous noradrenaline (Figure 2), prazosin did not significantly change the e.j.p. amplitudes (Figure 3, Table 1), although there was a slight tendency for the late e.j.ps in the train to be increased. Note that the initial e.j.ps had amplitudes similar to the depolarization evoked by exogenous noradrenaline (about 10 mV).

The effect of yohimbine 0.1 and 1 μM differed markedly from that of prazosin. Neither concentration changed the e.j.ps elicited by the first few pulses, but both concentrations clearly increased the response to the 4th and later pulses (Figure 4, Table 1). In the presence of yohimbine 0.1 and 1 μM a near-maximal e.j.p. amplitude was reached only with the 6th–7th pulse of the train, whereas in drug-free solution a steady-state was reached with the 3rd–4th pulse.

Table 1 Effects of drugs with affinity for α-adrenoceptors on the 1st and the 15th e.j.p. elicited by trains of 15 pulses at 3 Hz

Pretreatment of animals	*α-Adrenoceptor ligand* (μM)	n	*Amplitude of 1st e.j.p.* (mV) *Before addition of ligand*[b]	*After addition of ligand*[b]	*Amplitude of 15th e.j.p.* (mV) *Before addition of ligand*[b]	*After addition of ligand*[b]
—	—	4	9.3 ± 0.2	10.7 ± 0.9	17.5 ± 2.1	19.4 ± 2.3
—	Prazosin 0.5	6	9.8 ± 0.5	9.7 ± 0.8	18.3 ± 1.0	20.8 ± 1.5
—	Yohimbine 0.1	4	9.4 ± 0.7	10.6 ± 0.4	17.0 ± 2.6	26.6 ± 0.7*
—	1.0	6	9.2 ± 0.7	8.1 ± 0.7	18.6 ± 0.9	35.3 ± 2.6***
—	Rauwolscine 1.0	5	9.5 ± 1.0	9.5 ± 1.5	18.5 ± 1.0	31.9 ± 1.7***
—	Corynanthine 0.1	4	9.5 ± 0.5	10.6 ± 0.4	17.4 ± 1.1	17.8 ± 1.2
—	1.0	5	9.7 ± 0.1	9.6 ± 0.2	16.9 ± 0.8	23.3 ± 1.0**
—	Clonidine 0.01	5	9.2 ± 0.5	1.1 ± 0.1***	19.3 ± 0.9	7.5 ± 0.7***
Reserpine[a]	Yohimbine 1.0	5	9.2 ± 0.6	7.4 ± 0.4*	37.7 ± 2.8	35.9 ± 2.4
Reserpine[a]	Clonidine 0.01	4	9.9 ± 0.4	1.6 ± 0.4***	33.4 ± 1.4	9.0 ± 1.2***

[a] 5 mg/kg s.c. 48 h and 2.5 mg/kg i.p. 24 h before mice were killed.

[b] E.j.ps were elicited by two trains of 15 impulses each before and after the addition of the α-adrenoceptor antagonist or clonidine. E.j.p. amplitudes in the two corresponding trains were averaged.

Significant differences from amplitudes before addition of the α-adrenoceptor ligands: $*P<0.05$; $**P<0.01$; $***P<0.001$.

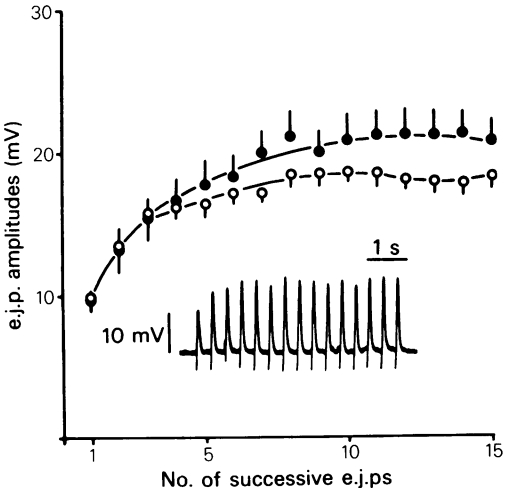

Figure 3 Effect of prazosin on the amplitudes of e.j.ps elicited by trains of pulses at 3 Hz in the mouse vas deferens. E.j.ps were elicited before (○) and after (●) the addition of prazosin 0.5 μM. Means of 6 experiments; s.e.means shown by vertical lines. Inset shows a typical record of e.j.ps before the addition of prazosin.

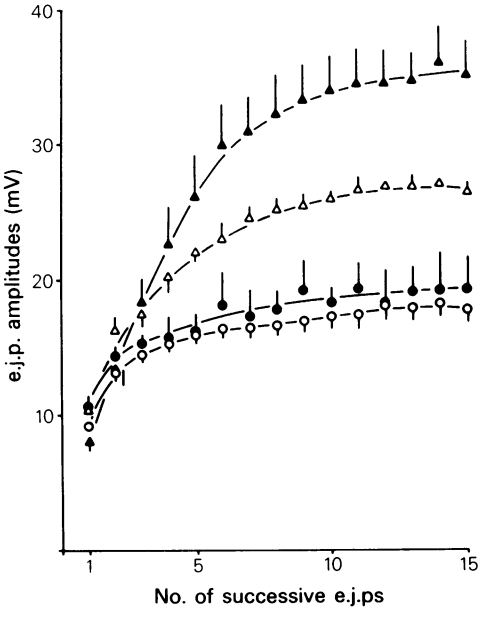

Figure 4 Effect of yohimbine on the amplitudes of e.j.ps elicited by trains of 15 pulses at 3 Hz. E.j.ps were elicited before (○, $n = 14$) and after the addition of either yohimbine 0.1 μM (△, $n = 4$) or 1 μM (▲, $n = 6$) or no drug (●, $n = 4$). Open circles represent the pooled e.j.p. amplitudes before the addition of either yohimbine or no drug. Mean values are shown with vertical lines indicating s.e.mean.

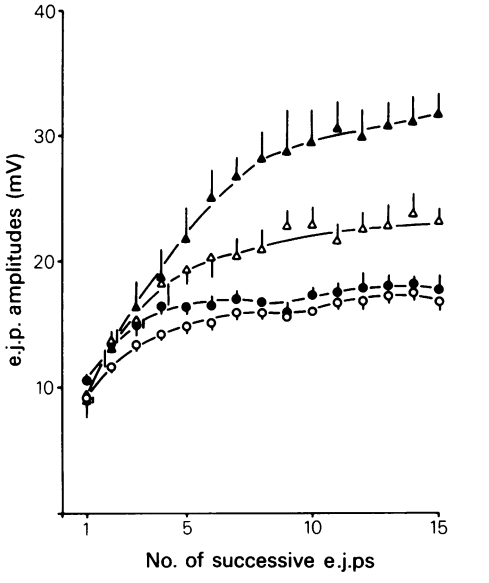

Figure 5 Effects of corynanthine and rauwolscine on the amplitudes of e.j.ps elicited by trains of 15 pulses at 3 Hz. E.j.ps were elicited before (○, $n = 14$) and after the addition of either corynanthine 0.1 μM (●, $n = 4$) or 1 μM (△, $n = 5$) or rauwolscine 1 μM (▲, $n = 5$). The open circles represent the pooled e.j.p. amplitudes before the addition of either corynanthine or rauwolscine. Mean values are shown with vertical lines indicating s.e.mean.

Experiments with the yohimbine diastereoisomers, rauwolscine and corynanthine, are illustrated in Figure 5. Rauwolscine 1 μM produced changes similar to yohimbine 1 μM. Corynanthine 0.1 μM did not enhance any e.j.p. amplitude. Although corynanthine 1 μM increased the amplitude of the 4th and subsequent e.j.ps, its effect was much smaller than that of the same concentration of yohimbine or rauwolscine (see also Table 1).

Interaction between clonidine and yohimbine on e.j.p. amplitudes

In order to study the interaction between clonidine and yohimbine, single e.j.ps were elicited by pulses set 30 s apart (Figure 6). Clonidine 0.01 μM strongly reduced the e.j.p. amplitudes and its effect was rapidly and completely antagonized by yohimbine 1 μM.

Effects of clonidine, yohimbine and reserpine-treatment on e.j.p. amplitudes

Finally, we studied e.j.ps in vasa deferentia from reserpine-treated mice. In these preparations a higher intensity of stimulation had to be used in order to evoke an e.j.p. of about 10 mV than in tissues from

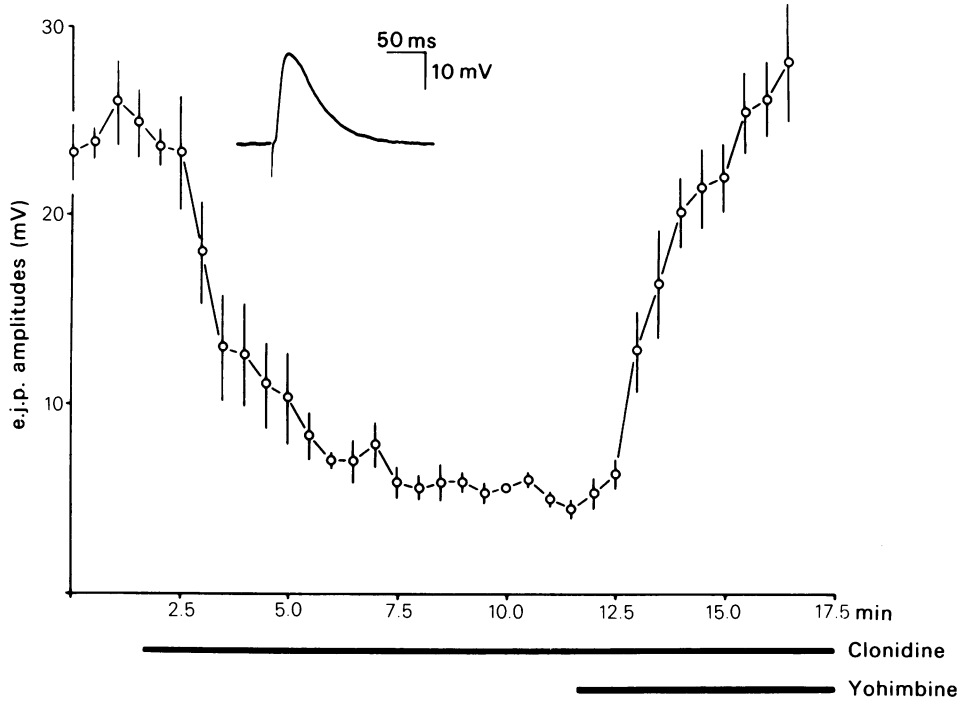

Figure 6 Interaction between clonidine and yohimbine on the amplitudes of e.j.ps elicited by single pulses at 30 s intervals. Clonidine 0.01 μM and yohimbine 1 μM were added to the superfusion medium as indicated. Means of 4 experiments; vertical lines indicate s.e.mean. Inset shows an e.j.p. before clonidine.

untreated animals. Figure 7 shows that the facilitation observed in tissues from reserpine-treated mice (open triangles) far exceeded that obtained in tissues from untreated animals (open circles). Clonidine 0.01 μM reduced the e.j.ps in both groups to approximately the same size (Figure 7, Table 1). In the untreated group, the percentage inhibition was larger for the first pulse than for all subsequent pulses. By contrast, in the reserpine-treated group, inhibition by clonidine declined only from the 7th pulse onwards. Yohimbine 1 μM failed to cause any further increase in e.j.p. amplitudes in tissues from reserpine-treated mice (Figure 7, Table 1). Similar results were obtained in tissues from animals pretreated with α-methyl-*p*-tyrosine in addition to reserpine (not shown).

Discussion

In the present experiments, iontophoretically applied noradrenaline, in contrast to bath-applied noradrenaline (Henderson & North, 1976), evoked reproducible depolarizations in the mouse vas deferens. Prazosin 0.5 μM, which abolished these local responses to noradrenaline, changed neither the spontaneous nor the nerve stimulation-induced e.j.ps. Since iontophoretic pulses of short duration failed to evoke a detectable depolarization, noradrenaline had to be ejected by pulses of rather long duration (2–3 s). It seems possible, therefore, that extrajunctional adrenoceptors (Hotta, 1969) of the α_1-type were reached by the amine. It has been known for some time that contractions (Ambache & Zar, 1971; Jones & Spriggs, 1975) or depolarizations (Burnstock & Holman, 1962; 1964; Holman, 1967) of the vas deferens elicited by bath-applied noradrenaline are sensitive to α-adrenoceptor antagonists, whereas responses evoked by nerve stimulation are highly resistant to these drugs. Possible reasons for this, such as the existence of a second motor transmitter in addition to noradrenaline, or of receptors distinct from α- or β-adrenoceptors, have been discussed (Jenkins *et al.*, 1977; Marshall *et al.*, 1978b; for further possible explanations see Furness, 1974). Dopamine may function as a neurotransmitter in certain postganglionic autonomic nerves (Bell, 1982) and the vas deferens contains considerable concentrations of dopamine (Z. Lacković & N.H. Neff, personal communication). However, it is unlikely that the second, non-noradrenergic transmitter, if any, is dopamine, because the spontaneous e.j.ps were resis-

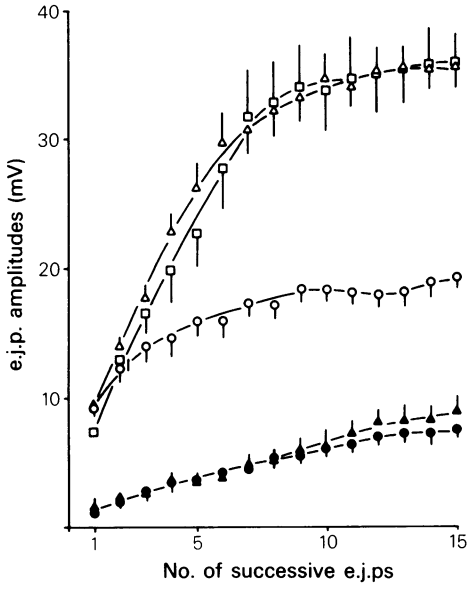

Figure 7 Effects of clonidine and yohimbine on the amplitudes of e.j.ps elicited by trains of 15 pulses at 3 Hz in vasa deferentia from normal and reserpine-treated mice. Tissues from normal mice (○, ●): e.j.ps were elicited before (○, $n = 5$) and after (●, $n = 5$) the addition of clonidine 0.01 μM. Tissues from reserpine-treated mice (△, ▲, □, see Methods): e.j.ps were elicited before (△, $n = 9$) and after the addition of either clonidine 0.01 μM (▲, $n = 4$) or yohimbine 1 μM (□, $n = 5$). The open triangles represent the pooled e.j.p. amplitudes in tissues from reserpine-treated mice before the addition of either clonidine or yohimbine. Mean values are shown with vertical lines indicating s.e.mean.

tant to high concentrations of the dopamine receptor antagonist, haloperidol. The reduction of noradrenaline-evoked depolarizations caused by haloperidol is probably due to an α-antagonist effect of this compound.

Whatever the nature of the motor transmitter(s) in the mouse vas deferens, our experiments clearly indicate that the release of the transmitter is inhibited by activation of presynaptic α-adrenoceptors. We have employed subtype-selective compounds, namely the α_2-agonist clonidine, the α_2-antagonists yohimbine and rauwolscine, and the α_1-antagonists corynanthine and prazosin (Starke, Montel, Gayk & Merker, 1974; Weitzell, Tanaka & Starke, 1979; see also Starke, 1981). Clonidine at a rather low concentration (0.01 μM) reduced the e.j.p. amplitudes, and its effect was counteracted by yohimbine 1 μM. Although we did not study the mode of this interaction, Blakeley *et al.* (1981) have shown that, in the guinea-pig vas deferens, the α-receptor blocking drug, piperoxan, antagonized the effect of clonidine in an apparently competitive manner. Moreover, our experiments indicate that the presynaptic α-adrenoceptors normally receive the input of an endogenous agonist, presumably noradrenaline. In support of this view, yohimbine and rauwolscine at low concentrations greatly increased the e.j.p. amplitudes from the 3rd impulse in a train onwards. Blakeley *et al.* (1981) have similarly shown that piperoxan, azapetine and prazosin increased e.j.p. amplitudes. These authors concluded that the antagonists enhanced the e.j.ps irrespective of their relative potencies at α_1- and α_2-adrenoceptors. We cannot agree with this conclusion because, at least in the mouse vas deferens, the α_2-selective antagonists, yohimbine and rauwolscine, were much more potent in increasing the e.j.ps than the α_1-selective diastereoisomer, corynanthine. Moreover, prazosin at up to 0.5 μM had no effect on the e.j.p.

Our results agree qualitatively with those of Bennett (1973) and Bennett & Middleton (1975b). These authors used very high concentrations (about 30 μM) of phenoxybenzamine, dibenamine, phentolamine, dihydroergocristine and dihydroergocornine. They obtained two effects: e.j.ps elicited by single pulses or the first pulses in trains were reduced. On the other hand, the depression that followed the initial facilitation in pulse trains at frequencies higher than 1 Hz was reversed to continuous facilitation until a steady-state was reached. Although we did not observe a secondary depression of e.j.ps with trains of 15 pulses at 3 Hz, the normal increase in e.j.p. amplitude was greatly enhanced by yohimbine and rauwolscine. In contrast to Bennett (1973) and Bennett & Middleton (1975b) we obtained this effect at antagonist concentrations which did not reduce the first e.j.ps (except yohimbine 1 μM in vasa deferentia of reserpine-treated mice).

Apart from the simple qualitative facilitatory effect of the α_2-antagonists, two observations indicate that the presynaptic α-adrenoceptors in the mouse vas deferens are the target of neurally released noradrenaline. First, the fact that the e.j.ps elicited by the first 2–3 pulses were not enhanced by yohimbine and rauwolscine is probably due to the necessity of a certain minimal concentration of released noradrenaline to accumulate in the vicinity of the presynaptic receptors. In agreement with this view, it has been demonstrated that in the mouse vas deferens yohimbine 0.01 or 0.1 μM failed to influence the release of [^{3}H]-noradrenaline elicited by a single pulse, whereas it increased the average release evoked by 2 or 10 pulses at a frequency of 1 Hz (Markievicz, Marshall & Nasmyth, 1980; Baker & Marshall, 1982).

Secondly, when the tissue noradrenaline stores are depleted by reserpine, the normal autoinhibition of noradrenaline release is weakened and the release-

enhancing effect of α-adrenoceptor antagonists reduced. This has been shown previously in experiments in which the overflow of [^{3}H]-noradrenaline or other constituents of the noradrenaline storage granules was studied (Enero & Langer, 1973; Cubeddu & Weiner, 1975; Dixon, Mosimann & Weiner, 1978). Our experiments show the same phenomenon electrophysiologically. Reserpine-treatment changed the e.j.p. trains in much the same way as did the addition of yohimbine or rauwolscine, presumably because the normal α-adrenergic inhibition was interrupted due to lack of noradrenaline. Moreover, the normal effect of yohimbine on the e.j.ps was now abolished, whereas the effect of clonidine was unchanged or even enhanced, indicating that the presynaptic receptor mechanism itself was intact.

The interpretation of the reserpine experiments as given here is not unequivocal. Tissues from reserpine-treated mice were stimulated at a higher voltage than normal tissues in order to excite a larger number of fibres and thereby obtain a similar initial e.j.p. amplitude (10 mV). Hence, the postsynaptic effect of the transmitter was approximately the same as in control tissues. Why then was the presynaptic autoinhibition, according to our interpretation, abolished? We have no definite answer. One possibility is of course, that a second, unknown transmitter contributed to the e.j.ps but not to the α-adrenergic presynaptic inhibition. Another possibility could be that because of the narrow junctional cleft in the vas deferens (Furness, 1974) even the low quantities of noradrenaline released from partly depleted varicosities sufficed to elicit a small postsynaptic response; since more varicosities were excited, this increased number of small responses may have yielded e.j.ps of normal amplitude. In contrast to postsynaptic α-adrenoceptors, the presynaptic α-receptors may be located at certain strategic points outside the junctional cleft, so that the high quantities of noradrenaline discharged from full vesicles were required to obtain effective concentrations.

When trains of pulses were evoked at 3 Hz, the largest percentage inhibition by clonidine occurred with the first pulse, and the inhibition gradually diminished thereafter. The depression of e.j.p. amplitudes by normorphine similarly depended on the number of pulses applied (Illes *et al.*, 1980), possibly because at a facilitated state of transmitter release the increased intracellular free Ca^{2+} counteracted the effect of the opiate (see also Illes, 1982). In the case of clonidine, an additional mechanism might operate. As the number of pulses increased, the exogenous agonist met with an increasing background autoinhibition by released noradrenaline, and this of course curtailed the scope for the effect of clonidine. In support of this view, the percentage inhibition caused by clonidine was much less dependent on the number of pulses in reserpine-treated preparations in which the autoinhibition was absent, than in preparations from untreated animals.

In conclusion, we have shown electrophysiologically that the release of the motor transmitter in the mouse vas deferens is inhibited by activation of presynaptic α-adrenoceptors. The receptors are of the α_2-type. As shown by the disinhibition caused by α-adrenoceptor antagonists or reserpinization, the receptors are normally activated by released noradrenaline.

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