Br. J. Pharmac. (1982), **76**, 603–611

HOMOGENEOUS AND NON-HOMOGENEOUS DISTRIBUTION OF INHIBITORY AND EXCITATORY ADRENOCEPTORS IN THE LONGITUDINAL MUSCLE OF THE GUINEA-PIG ILEUM

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1 The effects of adrenoceptor agonists and antagonists on spontaneous and evoked membrane activities of longitudinal muscle cells from different parts of the guinea-pig ileum were observed, using microelectrode methods.

2 Isoprenaline inhibited the generation of spikes in cells in the terminal (0–3 cm from the ileocaecal valve) and proximal (more than 50 cm from the ileocaecal valve) regions of the ileum, with no change on the membrane potential and ionic conductance of the membrane. These actions of isoprenaline were abolished by propranolol.

3 Noradrenaline and phenylephrine depolarized the membrane and increased both the spike frequency and ionic conductance of cell membranes of the terminal ileum, whereas noradrenaline and clonidine hyperpolarized the membrane, increased the ionic conductance of the membrane and inhibited the spontaneously generated spikes from cells of the proximal ileum. The excitatory effect of phenylephrine in the cells of the proximal ileum and the inhibitory effect of clonidine on cells of the terminal ileum were less pronounced.

4 The excitatory actions of noradrenaline or phenylephrine were antagonized by prazosin and phentolamine, but not by yohimbine, whereas the inhibitory actions of noradrenaline or clonidine were antagonized by yohimbine and phentolamine but not by prazosin.

5 The cholinergic e.j.ps evoked by field stimulation to the tissue were not affected by isoprenaline or phenyleprine but were inhibited by noradrenaline and clonidine, in both the terminal and proximal regions of the ileum. These actions of noradrenaline and clonidine were antagonized by yohimbine but not by prazosin.

6 The results indicate that in the myenteric plexus and longitudinal muscle tissues of the guinea-pig ileum there are prejunctional inhibitory (α_2), postjunctional inhibitory (α_2 and β) and postjunctional excitatory (α_1) adrenoceptors. The homogeneous distributions of prejunctional α_2- and postjunctional β-adrenoceptors in the ileum are responsible for inhibitions of cholinergic excitatory junction potentials (e.j.ps) and spontaneous spike activities, respectively. The density of distribution of the postjunctional α_1-adrenoceptors is higher in the terminal than in the proximal regions, and these distributions are reversed in the case of the postjunctional α_2-adrenoceptors. The postjunctional α_1-adrenoceptors are probably responsible for the membrane depolarization and α_2-adrenoceptors for the hyperpolarization induced by catecholamines.

Introduction

The inhibitory and excitatory actions of sympathomimetic amines in the small intestine of several mammalian species have been described (Ahlquist & Levy, 1959; Furchgott, 1960; Innes & Kohli, 1969; Kosterlitz, Lydon & Watt, 1970; Furness & Costa, 1974; Kažič, 1975; Bauer, 1976). There is considerable evidence that prejunctional α-adrenoceptors distributed on the cholinergic nerve terminals play an inhibitory role on the acetylcholine release from the intramural myenteric plexus (Kosterlitz *et al.*, 1970; Paton, Vizi & Zar, 1971; Drew, 1977), and that the postjunctional α-adrenoceptors present in the smooth muscle membrane mediate the relaxation of smooth muscles of the ileum (McDougal & West, 1952; Kosterlitz *et al.*, 1970). However, there is also evidence for the existence of inhibitory and excitatory postjunctional α-adrenoceptors, which participate in the contraction or relaxation in the guinea-pig ileum by catecholamines (Anderson & Lees, 1976; Bauer, 1976; Wikberg, 1978).

It has been recently found that the prejunctional

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0007-1188/82/080603-09 $01.00

inhibitory and postjunctional inhibitory adrenoceptors are homogeneously distributed in all regions of the guinea-pig ileum, whereas the postjunctional excitatory and inhibitory adrenoceptors have different densities of distribution in terminal and proximal regions of this tissue. However, these conclusions were derived mainly from observations of the mechanical responses of the ileum (Bauer 1980; 1981).

The present study was carried out to analyse the distributions of the adrenoceptors in the longitudinal muscle layer of the guinea-pig ileum using electrophysiological procedures. The effects of adrenoceptor agonists and antagonists on the membrane potential and spike activities evoked spontaneously or by electrical stimulation were observed in proximal and terminal regions of the longitudinal muscle layer of the guinea-pig ileum.

Methods

Guinea-pigs of either sex were stunned and bled. The ileum was incised along the mesentery; the lumen of the preparations was flushed with Krebs solution and the mucosal layer was carefully removed. Experiments were performed on the isolated terminal (0 to 3 cm from the ileocaecal valve) and proximal (more than 50 cm from the ileocaecal valve) ileum of the guinea-pig. Longitudinal strips of the tissue (about 15 mm in length and 1.5 mm in width) were prepared. The strips of the tissue were gently stretched and pinned on a rubber plate in an experimental chamber made from a lucite plate. The partition stimulating method (Abe & Tomita, 1968) was used for recording the electrotonic potential of muscle membranes. Field stimulation (0.05 to 0.15 ms pulse duration) was applied to activate nerve fibres, using a pair of Ag-$AgCl_2$ electrodes; one electrode was placed on the tissue 1 to 2 mm from the inserted microelectrode and the other one at a distance of 15 mm. To record the membrane activity of single longitudinal muscle cells, a conventional glass capillary microelectrode filled with 3 M KCl was used; the cells were impaled from the serosal surface. A chamber of 1.5 ml volume was superfused with warmed Krebs solution (36°C) at a rate of 3 to 4 ml/min. Modified Krebs solution of the following composition was used (mM): Na^+ 137.4, K^+ 5.9, Ca^{2+} 2.5, Mg^{2+} 1.2, Cl^- 134.0, HCO_3^- 15.5, $H_2PO_4^-$ 1.2 and glucose 11.5. The solutions were gassed with 97% O_2 and 3% CO_2, and the pH was maintained at 7.2 to 7.4.

The following drugs were used: atropine sulphate (Tanabe), clonidine hydrochloride, phenylephrine hydrochloride, hexamethonium chloride, yohimbine hydrochloride (Tokyo Kasei), isoprenaline hydrochloride (Sumitomo), noradrenaline hydrochloride (Sankyo), phentolamine mesylate (CIBA-Geigy), prazosin hydrochloride (Pfizer-Taito), propranolol hydrochloride (ICI), tetrodotoxin (TTX, Sigma). All concentrations are expressed as mol(base)/l (M). When the effects of adrenoceptor agonists were studied in the presence of adrenoceptor antagonists, the antagonist was applied at least 15 min before the agonists.

The results are expressed as the mean ± s.e.mean. Student's t test was used to evaluate the statistical significance of results (Delaunois, 1973).

Results

Membrane potential and spontaneous activity

The mean resting membrane potentials of longitudinal muscle cells of the terminal and proximal ileum were -52.4 ± 0.62 ($n = 103$) and -53.3 ± 0.56 ($n = 79$), respectively. In the longitudinal muscle cells of both regions, most of the cells generated spontaneous spikes with after-hyperpolarization, either continuously or as bursts between silent periods.

Isoprenaline (0.3 to 1 μM) did not change the membrane potential and membrane resistance of the longitudinal muscle cells in the terminal ($n = 5$) and proximal ($n = 7$) ileum but did decrease concentration-dependently the frequency of the spontaneously generated spikes. With application of 1 μM isoprenaline, the generation of spontaneous spikes was abolished (Figure 1a). Treatment with propranolol (0.5 μM) did not modify the membrane potential or the spike generation but did block completely the action of the subsequently applied isoprenaline on the spike activity (Figure 1b). The action of isoprenaline was not affected by pretreatment with phentolamine (1 μM).

To observe the effects of catecholamines on the α-adrenoceptors, preparations were pretreated with propranolol (0.5 μM) throughout the following experiments.

In cells of the terminal ileum, noradrenaline (0.1 to 10 μM) depolarized the membrane and increased the spike frequency, concentration-dependently (Figure 2a), whereas in cells of the proximal ileum, this agent hyperpolarized the tissue and inhibited the generation of spontaneous spike activities (Figure 3a).

Yohimbine (0.5 and 1 μM) slightly depolarized the membrane in cells of both the proximal and terminal regions, and increased the frequency of spontaneous spikes. In the presence of yohimbine, the actions of noradrenaline (1 μM) were not affected in cells of the terminal ileum (Figure 2c), whereas in cells of the proximal ileum the noradrenaline-induced hyper-

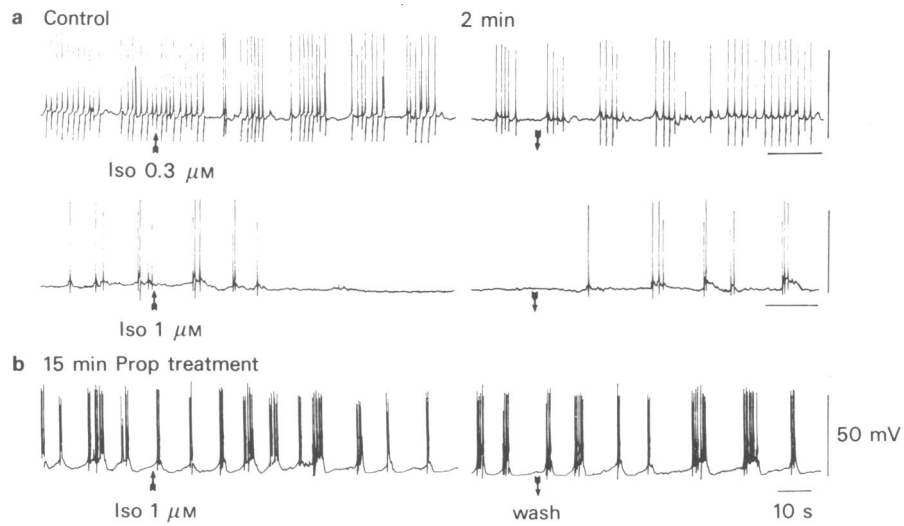

Figure 1 Effects of isoprenaline on the spontaneous membrane activity of the longitudinal muscle cells of the guinea-pig proximal ileum. (a) Control responses of two different cells to isoprenaline (Iso 0.3 and 1 μM); (b) effect of isoprenaline (μM) after 15 min propranolol (Prop 0.5 μM) treatment. Records are before, during (2 min) and after application of isoprenaline. The last two records are from the same cell but on different time scales. Application (↓) and washout (↓) of isoprenaline are indicated.

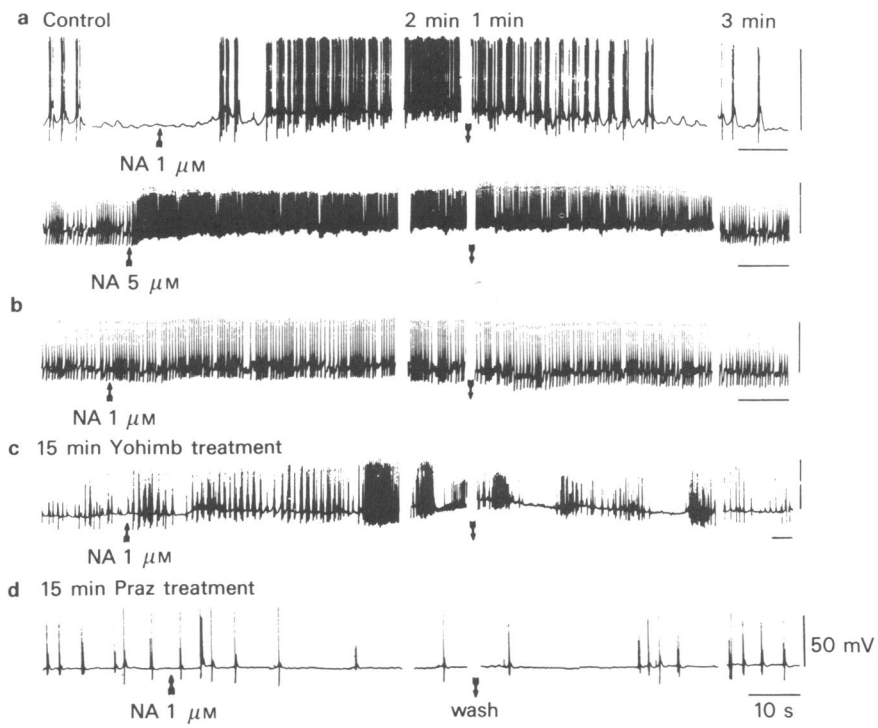

Figure 2 Effects of noradrenaline on the spontaneous membrane activity of the longitudinal muscle cells of the guinea-pig terminal ileum. (a) control responses of two different cells to noradrenaline (NA 1 and 5 μM); (b), (c) and (d) effects of noradrenaline (1 μM) after 15 min phentolamine (Phent 1 μM), yohimbine (Yohimb 1 μM) or prazosin (Praz 1 μM) treatment. Records are before, during (2 min) and after (1 and 3 min) application of noradrenaline. Records (c) and (d) are taken from the same cell. Propranolol (0.5 μM) was present throughout the experiments. Application (↓) and washout (↓) of noradrenaline are indicated.

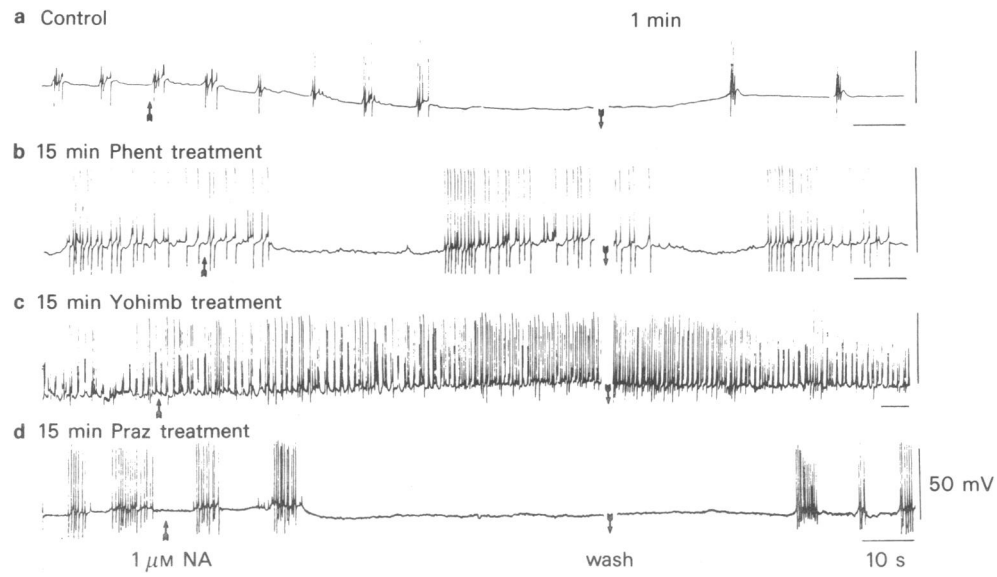

Figure 3 Effects of noradrenaline on the spontaneous membrane activity of the longitudinal muscle cells of the guinea-pig proximal ileum. (a) Control response to noradrenaline (NA 1 μM); (b), (c) and (d) effects of noradrenaline (1 μM) after 15 min phentolamine (Phent 1 μM), yohimbine (Yohimb 1 μM) and prazosin (Praz 1 μM) treatment, respectively. Records are taken before, during and 1 min after application of noradrenaline. Propranolol (0.5 μM) was present throughout the experiments. Application (↓) and washout (↓) of noradrenaline are indicated.

polarization in the control solution reversed the polarity to a slight depolarization with an accompanied increase in the spike frequency (Figure 3c). Prazosin (1 μM) slightly hyperpolarized the membrane and decreased the spontaneous spike activity. After application of prazosin, the noradrenaline-induced depolarization of cells of the terminal ileum was no longer observed (Figure 2d); however, prazosin did not affect the action of noradrenaline on the cells of the proximal ileum (Figure 3d). Phentolamine (1 μH7M) inhibited both the excitatory and inhibitory actions of noradrenaline (1 μM) on cells in both the terminal and proximal ileum (Figures 2b, 3b).

Figure 4 summarizes the effects of noradrenaline (0.1 to 10 μM) on the membrane potential of the cells of terminal and proximal ileum before, and during treatment with yohimbine (1 μM) or prazosin (1 μM). In cells of the terminal ileum, yohimbine slightly shifted to the left the noradrenaline-induced concentration-response curve, whereas in cells of the proximal ileum, this agent shifted the concentration-response curve to noradrenaline to the right, and reversed the polarity from hyperpolarization to depolarization in the case of lower concentrations of noradrenaline (0.1 to 1 μM). In contrast, prazosin (1 μM) shifted the noradrenaline-induced dose-response relationship to the right in cells of the terminal ileum, and changed the membrane polarity from depolarization to hyperpolarization in the presence of noradrenaline (0.3 to 1 μM). In cells of the proximal ileum, however, prazosin (1 μM) had little effect on the action of noradrenaline (0.1–3 μM). When a high concentration of noradrenaline (10 μM) was applied to the tissue in the presence of prazosin (1 μM), the membrane was hyperpolarized to a greater extent by noradrenaline than was the control, due to inhibition of the noradrenaline-induced depolarization.

Phenylephrine (50 μM) depolarized the membrane, reduced the membrane resistance and increased the frequency of spontaneous spikes, whereas clonidine (10 μM) hyperpolarized the membrane and inhibited the spontaneously generated spikes. The effects of phenylephrine appeared more predominantly in the cells from the terminal regions than in those from the proximal regions. These actions of phenylephrine were prevented by pretreatment with prazosin (1 μM) but were not affected by pretreatment with yohimbine (1 μM). Clonidine hyperpolarized the membrane in cells of the proximal ileum to a greater extent than was seen in the terminal ileum, and these hyperpolarizing actions were inhibited by pretreatment with yohimbine but not by prazosin (Table 1).

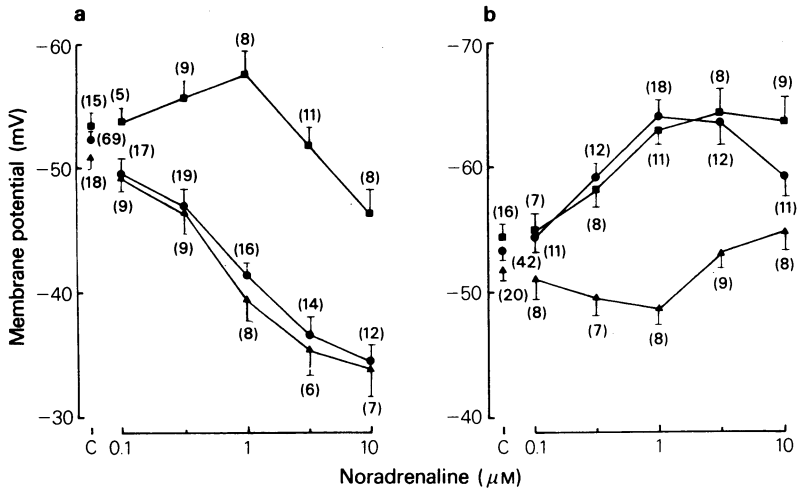

Figure 4 Effects of noradrenaline and α-adrenoceptor antagonists upon the membrane potentials of the guinea-pig terminal (a) and proximal ileum (b). C: control; membrane potential before application of noradrenaline. Membrane potential changes induced by noradrenaline: (●); noradrenaline actions on the membrane potential under treatment with prazosin (1 μM): (■); effects of noradrenaline on the membrane under treatment with yohimbine (1 μM): (▲). Propranolol (0.5 μM) was present in the bathing solution throughout the experiments. Each point represents the mean; vertical lines show the s.e. Number of trials is given in parentheses. Ordinates membrane potential; abscissae, concentration of noradrenaline.

Effects of catecholamines on the response of the ileum to field stimulation

During the silent periods between the bursts of spikes, applications of field stimulation (0.05 to 0.15 ms) produced a depolarization of the membrane. In most of the cells, spikes were superimposed on the depolarization. The membrane depolarization and spike activity evoked by field stimulation were unaffected by hexamethonium (up to 10 μM) ($n = 5$), but ceased after either atropine (1 μM) or TTX (0.3 μM). Thus, the membrane depolarization in-

Table 1 Changes in the membrane potential induced by α-adrenoceptor agonists and antagonists

	Terminal ileum	*Proximal ileum*
	Membrane potential in mV [mean ± s.e.] (n)	
Control	−52.1 ± 0.70 (34)	−53.0 ± 0.62 (37)
Phenylephrine 50 μM	−39.3 ± 1.52 (21)*	− 46.5 ± 1.64 (9)*
Clonidine 10 μM	−56.4 ± 1.62 (8)	−62.2 ± 1.53 (11)*
Yohimbine 1 μM	−50.3 ± 0.88 (12)	−51.1 ± 1.04 (10)
Prazosin 1 μM	−54.5 ± 0.97 (11)	−55.8 ± 0.92 (12)
Yohimbine 1 μM + phenylephrine 50 μM	−38.5 ± 2.16 (8)*	−45.7 ± 1.20 (7)*
Prazosin 1 μM + phenylephrine 50 μM	−51.2 ± 0.99 (9)†	−54.3 ± 1.04 (9)†
Yohimbine 1 μM + clonidine 10 μM	− 51.6 ± 1.07 (7)	−54.1 ± 1.76 (9)†
Prazosin 1 μM + clonidine 10 μM	−59.8 ± 1.45 (8)*	−63.7 ± 1.64 (8)*

*Significantly different from the control ($P < 0.05$).
†Significant difference in comparison to the response in the absence of α-adrenoceptor antagonist ($P < 0.05$).

duced by field stimulation is due to excitations of the peripheral cholinergic nerve fibres and is an excitatory junction potential (e.j.p.). Noradrenaline (0.1 to 1 μM) either reduced the amplitude or abolished the generations of e.j.ps and spike activity superimposed on e.j.p., due to single pulse field stimulation in cells of both the proximal and the terminal regions of the longitudinal muscle of the guinea-pig ileum (Figure 5). Responses of the membrane induced by high frequencies of stimulation (5 pulses, 20 Hz) were little affected by noradrenaline (1 μM) (not shown in the Figure).

Noradrenaline, in concentrations over 0.1 μM, reduced the input resistance of the cell membrane of both the terminal and proximal ileum, but this agent depolarized or hyperpolarized the membrane in cells of the terminal or proximal ileum. The concentration-dependent inhibition of e.j.ps induced by noradrenaline is, in part, related to the reduction in the input resistance of the membrane. In the presence of noradrenaline (1 to 10 μM), the e.j.p. evoked by field stimulation ceased, whereas direct muscle stimulation continued to elicit spikes, albeit with reduction in the number evoked. The α-adrenoceptor antagonists, yohimbine (0.5 μM) and prazosin (1 μM), had little effect on the amplitude of e.j.ps. Prazosin (1 μM) slightly inhibited the action of noradrenaline on e.j.ps and yohimbine (0.5 μM) shifted the dose-dependent inhibition on the e.j.ps to the right (Figure 6).

Phenylephrine (5 to 50 μM) had no effect on the e.j.ps ($n = 6$), whereas clonidine (1 to 10 μM) inhibited or completely blocked the generation of e.j.ps evoked by a single pulse. Although clonidine had little effect on the generation of e.j.ps induced by repetitive stimulation (5 pulses, 20 Hz), the inhibitory effect of this drug on e.j.ps to single pulse field stimulation was prevented by yohimbine (0.5 μM) and was not affected by 1 μM prazosin (Figure 7).

When observing the effects of isoprenaline (0.1 to 1 μM) on the e.j.ps, propranolol was omitted from the bathing solution. This drug had no effect on the amplitude of e.j.ps ($n = 6$).

Discussion

In the guinea-pig ileum, distribution of at least three different subtypes of adrenoceptors has been elucidated, namely inhibitory postjunctional β-, inhibitory

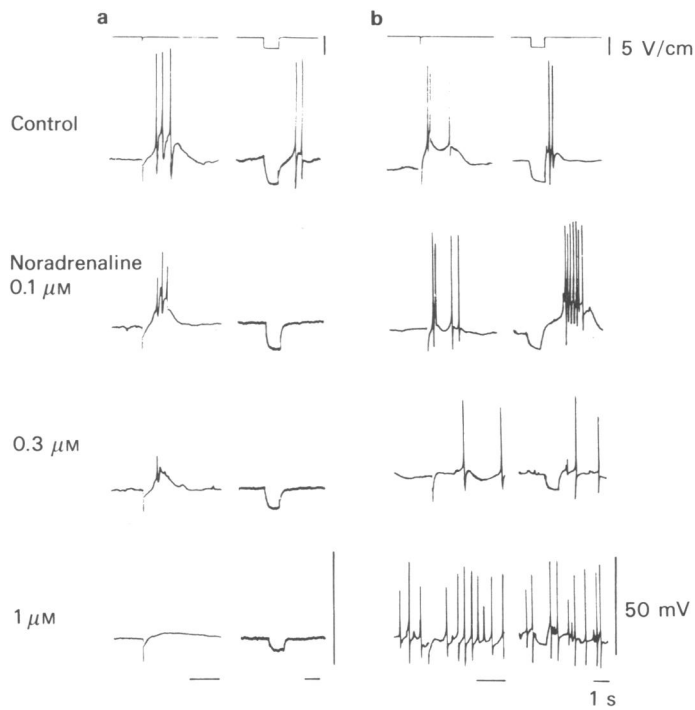

Figure 5 Effects of noradrenaline on cholinergic e.j.ps and electrotonic potentials evoked by inward current pulses (1 s pulse duration) in the cells of the guinea-pig proximal and terminal ileum. Records are before and 2 min after application of noradrenaline (0.1, 0.3 and 1 μM) to the same cell of proximal (a) or terminal (b) ileum, respectively. Propranolol (0.5 μM) was present throughout the experiments.

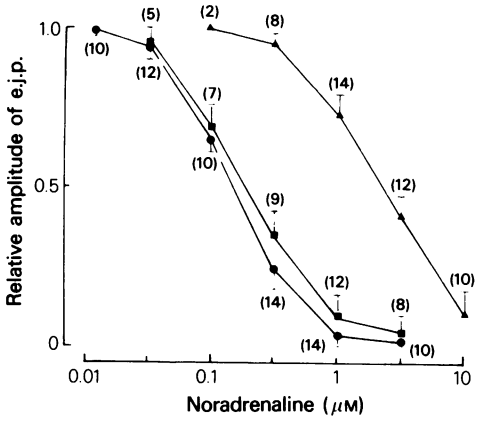

Figure 6 Effects of noradrenaline and α-adrenoceptor antagonists on the cholinergic e.j.ps of proximal ileum. Inhibition of e.j.ps by noradrenaline: (●); during the presence of prazosin (1 μM): (■) and during the presence of yohimbine (0.5 μM): (▲). Propranolol (0.5 μM) was present throughout the experiments. Each point represents the mean; vertical lines show s.e.mean; number of trials is given in parentheses. Ordinate scale: relative amplitude of e.j.ps (control response before application of drugs was taken as unity); abscissa scale: concentration of noradrenaline.

prejunctional and postjunctional α- and excitatory post junctional α-adrenoceptors (Kosterlitz *et al.*, 1970; Anderson & Lees, 1976; Drew, 1977; Wikberg, 1978). Based on the actions of adrenoceptor agonists and antagonists on the mechanical activity of different segments of the guinea-pig ileum, regional differences in the distribution of adrenoceptors were postulated (Bauer, 1981).

The inhibitory effect of isoprenaline predominantly resulted in an activation of postjunctional β-adrenoceptors, because this agent did not modify the amplitude of e.j.ps and this action was blocked by propranolol but not by phentolamine. There was no difference in the actions of isoprenaline on cells obtained from different regions of the guinea-pig ileum, thus confirming the previous observation that the inhibitory postjunctional β-adrenoceptors are distributed homogeneously in the longitudinal muscle layer of the guinea-pig ileum (Bauer, 1981). The inhibition of spike generation in the longitudinal muscle cells of the guinea-pig ileum with isoprenaline was not associated with either changes in the membrane potential or membrane conductance. Such actions of isoprenaline have been reported in the case of the guinea-pig taenia coli (Bülbring & Kuriyama, 1973; Bauer & Zakhari, 1977; Bülbring & Den Hertog, 1980).

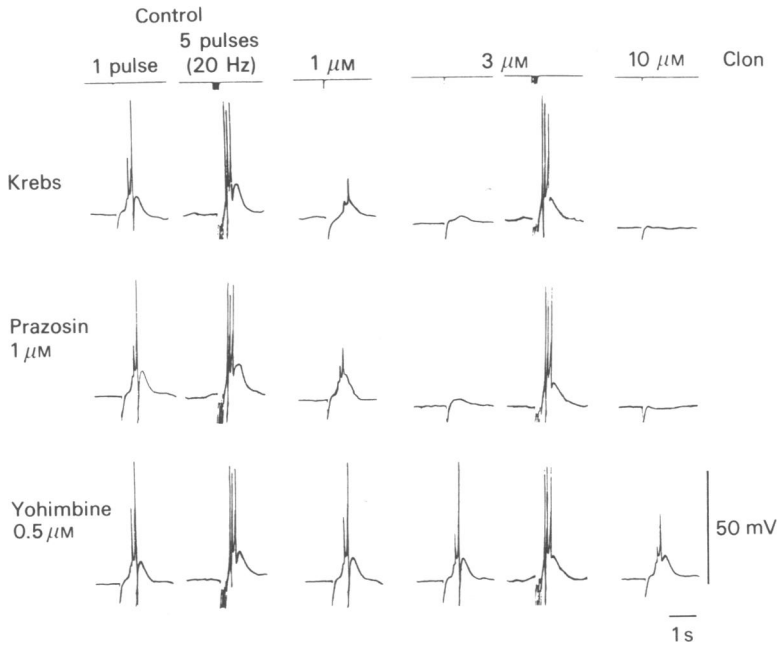

Figure 7 Effects of clonidine on cholinergic e.j.ps evoked from longitudinal muscle cells of the guinea-pig proximal ileum. Records are taken before and during application of clonidine (Clon 1, 3 and 10 μM) for 3 min in the Krebs solution and following 15 min pretreatment with prazosin (1 μM) or yohimbine (0.5 μM). E.j.ps were elicited by single and repetitive (5 pulses, 20 Hz) field stimulation. The concentration of clonidine and α-adrenoceptor antagonists and the number of pulses applied are indicated.

Subtypes of α-adrenoceptors are classified according to sensitivities to agonists and antagonists. In the present study, noradrenaline and phentolamine (nonselective agonist and antagonist), clonidine and yohimbine (α_2-adrenoceptor agonist and antagonist) and phenylephrine and prazosin (α_1-adrenoceptor agonist and antagonist) were used (Starke, Endo & Taube, 1975; Borowski, Starke, Ehrl & Endo, 1977).

The excitatory postjunctional α-adrenoceptors are more densely distributed in the terminal than in the proximal regions of the longitudinal muscle layer of the guinea-pig ileum (Bauer, 1981). However, we found that these receptors were also distributed in the proximal region and could be revealed after blockade of the postjunctional inhibitory α-adrenoceptors. Since the membrane depolarization and increased spike activity were induced by noradrenaline or phenylephrine but not by clonidine, and the actions of noradrenaline and phenylephrine were prevented by prazosin or phentolamine but not by yohimbine, the postjunctional excitatory α-adrenoceptors could be classified as an α_1-adrenoceptor subtype. Such a distribution of excitatory α-adrenoceptors resembles that seen in the ileocaecal sphincter of the guinea-pig (M. Kubota, personal communications).

The activation of α_1-adrenoceptors in the longitudinal muscle cells of the guinea-pig ileum led to a depolarization, increased spike activity and increased in the membrane conductance, as has been observed in other smooth muscles, e.g. uterus, ileocaecal sphincter (Bülbring & Szurszewski, 1974; Kawarabayashi & Osa, 1976; Kawarabayashi, 1978; Kubota, personal communications). It was also suggested that the membrane depolarization, due to the action of catecholamines, is the result of an increased membrane conductance for Na^+, K^+ and in some tissues also for Cl^- (Magaribuchi, Ito & Kuriyama, 1971; Bülbring & Szurszewski, 1974; Bülbring & Tomita, 1977).

The inhibitory postjunctional α-adrenoceptors are more densely distributed in the proximal than in the terminal regions of the guinea-pig ileum. Since the membrane hyperpolarization and inhibition of spike activity are produced by noradrenaline or clonidine but not by phenylephrine, and these inhibitory actions are antagonized by yohimbine or phentolamine but not by prazosin, the postjunctional inhibitory α-adrenoceptors can be classified as α_2-adrenoceptors. The postjunctional inhibitory effects of catecholamines mediated by these α_2-adrenoceptors in the longitudinal muscle cells of the guinea-pig ileum were similar to those observed on the guinea-pig taenia coli (Bülbring & Tomita, 1969; 1977; Bauer & Zakhari, 1977).

The membrane depolarization induced by the field stimulation was the result of activation of peripheral cholinergic neurones, because it was not affected by hexamethonium and was blocked by atropine or TTX. Noradrenaline and clonidine inhibited these cholinergic e.j.ps induced by field stimulation and effects of these drugs were recorded from all areas of the ileum, thereby indicating a homogeneous distribution of presynaptic adrenoceptors. The inhibition of e.j.ps induced by α_2-adrenoceptor agonists is probably due to a reduction in the input resistance of the membrane and also in the reduction in acetylcholine release, as indicated by the action of catecholamine on the amount of released acetylcholine, measured by the bioassay method (Paton *et al.*, 1971; Vizi, 1974). Furthermore, phenylephrine reduced the membrane resistance but did not affect the amplitude of e.j.ps evoked by field stimulation.

The e.j.ps elicited by repetitive stimulation at a higher frequency were more resistant to the action of noradrenaline or clonidine than were those induced by a single stimulus. Such differences in the inhibitory actions were noted with regard to the actions of catecholamines and acetylcholine release (Vizi, 1974), and on the muscle contractions of the guinea-pig ileum (Bauer, Matušák & Kuriyama, 1982). Since the sensitivity of prejunctional inhibitory adrenoceptors to noradrenaline, clonidine and yohimbine is high while that to phenylephrine, prazosin, isoprenaline and propranolol is low, these receptors can be classified as α_2-adrenoceptors. Furthermore, the prejunctional inhibitory α_2-adrenoceptors possessed a higher sensitivity to noradrenaline than did the postjunctional excitatory and inhibitory adrenoceptors. This means that the presynaptic α_2-adrenoceptors distributed on cholinergic nerve terminals may play an important role in physiological conditions which regulate the muscle tone rather than the postjunctional inhibitory or excitatory adrenoceptors distributed on the muscle membranes.

It appears from these results that in the myenteric plexus and longitudinal smooth layer of the guinea-pig ileum, there is a homogeneous distribution of both inhibitory prejunctional α_2- and postjunctional β-adrenoceptors and that these receptors may be responsible for inhibition of acetylcholine release and inhibition of the generation of spontaneous spikes, respectively. The distribution of postjunctional α_2-adrenoceptors in the longitudinal muscle layer of the guinea-pig ileum is not homogeneous, e.g. there is a higher density of the excitatory (α_1) and lower density of inhibitory (α_2)-adrenoceptors in the terminal regions than in the proximal regions of the ileum. The activation of postjunctional α_1- and α_2-adrenoceptors is probably responsible for the membrane depolarization and hyperpolarization elicited by exogeneous and endogeneous adrenoceptor agonists in the guinea-pig ileum.

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(*Received March 16, 1982.*)