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THE ROLE OF THE HYPOGASTRIC NERVE IN BLADDER AND URETHRAL ACTIVITY OF THE DOG

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1 Stimulation of the hypogastric nerves increased the pressure in both the bladder and urethra of anaesthetized female dogs.

2 The responses were reduced but not abolished by the α-adrenoceptor antagonist phentolamine, whereas the β-adrenoceptor antagonist propranolol was either without effect or increased the responses. Atropine, methysergide and hexamethonium were without effect.

3 Close arterial injection of phenylephrine increased and isoprenaline decreased urethral pressure but both produced only a slight increase in bladder pressure.

4 Hypogastric nerve stimulation reduced subsequent responses of the bladder and urethra to pelvic nerve stimulation or to close arterial injection of acetylcholine. Isoprenaline, but not phenylephrine, also had an inhibitory action and 5-hydroxytryptamine enhanced the responses.

5 In the presence of hexamethonium the inhibitory action of isoprenaline still occurred but 5-hydroxytryptamine no longer enhanced the responses, suggesting that 5-hydroxytryptamine acts on the ganglia and isoprenaline acts, at least partially, on smooth muscle.

6 These results suggest that the role of the hypogastric nerves may be to modify inputs to the bladder and urethra as well as to act directly on the smooth muscle.

Introduction

The bladder and urethra are innervated by hypogastric and pelvic nerves. From experiments on a number of species, it has been concluded that 'the hypogastrics facilitate retention of urine by constricting the urethra and inhibiting the tone of the detrusor urinae' (Elliott, 1907). However, questions still remain as to the site of action and the nature of the nerve fibres. The hypogastric nerves are believed to be predominantly adrenergic (Taira, 1972) though in some species cholinergic and other nerve types have been identified (guinea-pig: Mantegazza & Naimzada, 1967; rat: Alm & Elmer, 1975). Pharmacological experiments indicate that the action of the adrenergic transmitter, noradrenaline, on the lower urinary tract can be separated into a contractile action via α-adrenoceptors and an inhibitory action via β-adrenoceptors (Edvardsen & Setekleiv, 1968). The predominance of α-receptors in the bladder neck and urethra and β-receptors in the detrusor (Nergårdh & Boréus, 1972; Awad, Bruce, Carro-Ciampi, Downie, Lin & Marks, 1974) could explain Elliott's observations. However, there are few adrenergic nerves to the smooth muscle cells of the bladder of the cat (Gosling & Dixon, 1975) and yet hypogastric nerve stimulation can produce a powerful contraction of the bladder (Edvardsen & Setekleiv, 1968). This suggests that either other nerve types are present or the actions are indirect.

As well as acting on the smooth muscle, the hypogastric nerves could act on ganglion cells in the pelvic plexus or on the blood vessels. Adrenergic nerves have been shown to end on the ganglion cells (Hamberger & Norberg, 1965) and there is some evidence in the bladder that hypogastric nerve stimulation in the cat (de Groat & Saum, 1972) or close arterial injection of drugs in the guinea-pig (Dave & Dhattiwala, 1976) modifies the responses produced by pelvic nerve stimulation. The vascular component of the intra-urethral pressure was shown to be small in the dog (Raz & Caine, 1972; Tulloch, 1974).

The present experiments were carried out on the dog to determine whether there is direct innervation of the bladder by the hypogastric nerves and whether hypogastric nerve activity can modify pelvic nerve inputs to the bladder in this species. Simultaneous records were taken of the urethral pressure in order to record any similar interaction between pelvic and hypogastric nerves and to observe the extent to which the bladder and urethra act as a single unit.

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Methods

Adult female dogs, ranging in weight from 11 to 24 kg, were used in these experiments. Anaesthesia was induced by intravenous injection of pentobarbitone sodium (Nembutal, 30 mg/kg body wt.) and maintained with nitrous oxide supplemented with further Nembutal if necessary. A cannula was inserted into the femoral artery so that the systemic arterial blood pressure could be monitored throughout an experiment.

Bladder and urethral pressures were measured by introducing 3 ureteric catheters through the urethral meatus. These were connected via Statham pressure transducers (P23) to a Grass polygraph (7C) and perfused continuously with 0.9% w/v NaCl solution (saline) at 0.1 ml/min (Creed & Tulloch, 1978). Urethral pressures were measured in the proximal (U_1) and middle (U_2) thirds of the urethra. The hypogastric and pelvic nerves were identified and divided on both sides. The distal ends of the divided nerves were stimulated with trains of pulses of 1 ms pulse width at 10 Hz for 10 or 30 s.

Drugs, introduced through a cannula into the urogenital branch of the internal iliac artery, included acetylcholine chloride (Hopkins and Wilkins), noradrenaline bitartrate (Winthrop), phenylephrine hydrochloride (Winthrop), isoprenaline hydrochloride (Winthrop) and 5-hydroxytryptamine (Sigma). Drugs injected into the systemic circulation via the femoral vein included phentolamine mesylate (CIBA), propranolol hydrochloride (ICI), hexamethonium bromide (Sigma), methysergide bimaleate (Sandoz), quinidine gluconate (Drug Houses of Australia) and atropine sulphate (Knoll).

Pressure increases produced in response to nerve stimulation or to acetylcholine were measured before and after injection of agonist or antagonist drugs. The paired values were compared by Student's t test.

Results

Hypogastric nerve stimulation and the effects of catecholamines

Stimulation of the hypogastric nerves normally resulted in an increase in pressure in both the bladder and urethra (Figure 1). The bladder response ranged from 0 to 12 mmHg (mean $\pm$ s.d. = 3.8 $\pm$ 2.8 in 35 animals), and was always less than half that produced by pelvic nerve stimulation (6 to 44%). Compared with the pelvic response it was poorly maintained and the pressure reached a peak within 5 s before declining towards the resting level. If stimulation was continued there was usually a steady pressure slightly

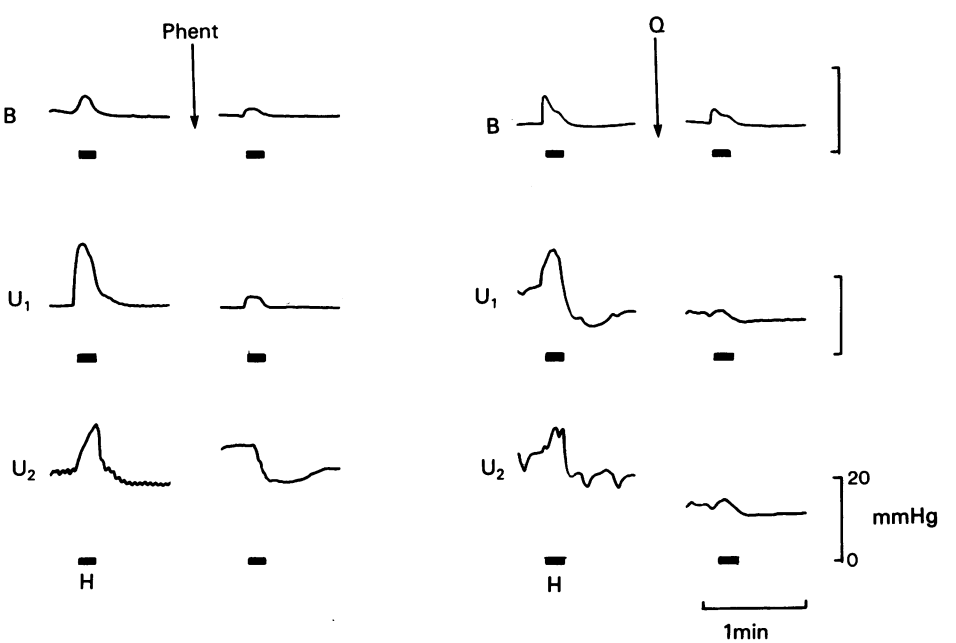

Figure 1 The pressure changes in the bladder (B) and 2 regions of the urethra (U) in 2 dogs produced by bilateral hypogastric nerve stimulation (H) for 10 s at 10 Hz. All responses were reduced by phentolamine (Phent, 1 mg/kg body wt.) and by quinidine (Q, 36 mg/kg body wt.).

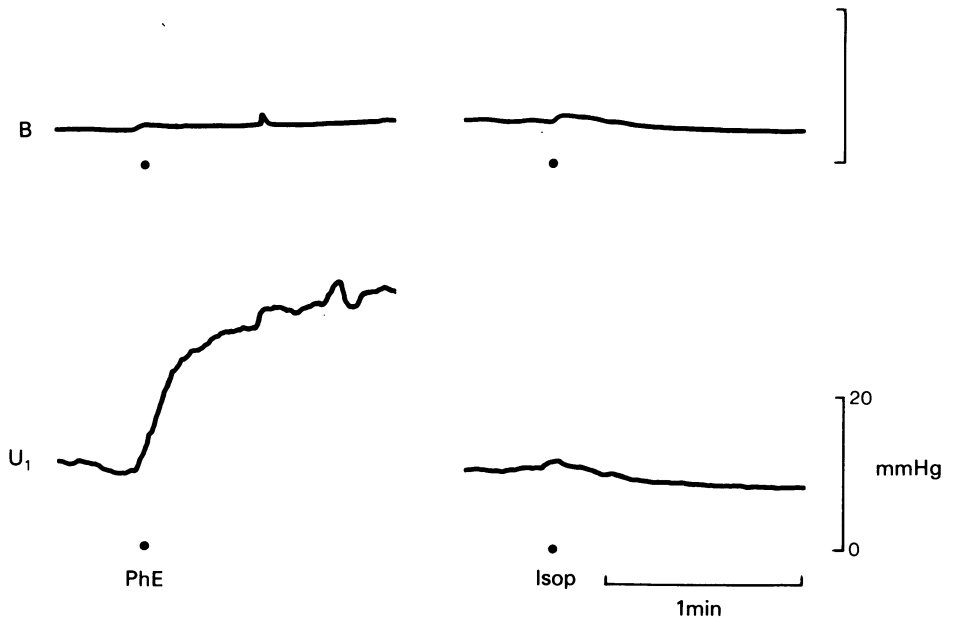

Figure 2 The effects of close arterial injection of phenylephrine (PhE, 20 μg) and isoprenaline (Isop, 20 μg). Both drugs produced only a slight increase in bladder pressure. Phenylephrine increased the urethral pressure and isoprenaline reduced it.

above the resting level which was rapidly restored when stimulation ceased.

The initial response of the urethra to hypogastric nerve stimulation was an increase in pressure ($U_1 = 8.4 \pm 4.5$; $U_2 = 6.9 \pm 4.0$ mmHg in 35 animals). However, its rise was slower than that of bladder and was often maintained more completely or continued to rise during the whole period of stimulation. At the end of stimulation the pressure did not return immediately to the resting level. In some animals there was a period of spontaneous activity while in others, especially those where the pressure was already high, the contraction was followed by relaxation to below the resting level. The pressure normally returned to the resting level within 1 to 4 min.

Close arterial injection of noradrenaline (10 μg) produced a biphasic response of the urethra which could be explained by the α and β actions of the adrenergic transmitter since the α-adrenoceptor agonist, phenylephrine, (10 to 20 μg) caused a rapid increase in pressure whereas injection of the β-adrenoceptor agonist, isoprenaline, (10 to 20 μg)

Table 1 The effect of drugs on the pressure responses of the urethra and bladder to hypogastric nerve stimulation

	Urethra				*Bladder*			
	Control (mmHg)	*After drug (mmHg)*	P	n	*Control (mmHg)*	*After drug (mmHg)*	P	n
Phentolamine	4.4 ± 4.8	−0.6 ± 2.3	***	21	3.0 ± 1.9	1.6 ± 1.3	**	13
Propranolol	4.8 ± 8.5	10.8 ± 12.3	*	9	8.1 ± 7.7	7.7 ± 6.7	NS	9
Atropine	10.4 ± 6.4	8.2 ± 5.8	NS	15	4.4 ± 5.0	2.8 ± 3.5	NS	9
Hexamethonium	6.4 ± 3.2	6.6 ± 2.7	NS	11	4.2 ± 2.9	3.6 ± 2.2	NS	7
Methysergide	5.8 ± 4.3	5.3 ± 3.5	NS	13	8.3 ± 4.7	10.4 ± 3.2	NS	8
Quinidine	7.9 ± 4.0	3.0 ± 1.6	**	12	3.4 ± 1.6	1.8 ± 1.0	*	7

Supramaximal hypogastric nerve stimulation at 10 Hz was used. Measurements were taken before and after injection of the antagonist drug into the femoral vein and the results compared by Student's t test. No other antagonist drugs had previously been given. Probability (P) *** = <0.001, ** = <0.01, * = <0.05 NS = not significant. Values shown are mean ±s.d. n = number of observations.

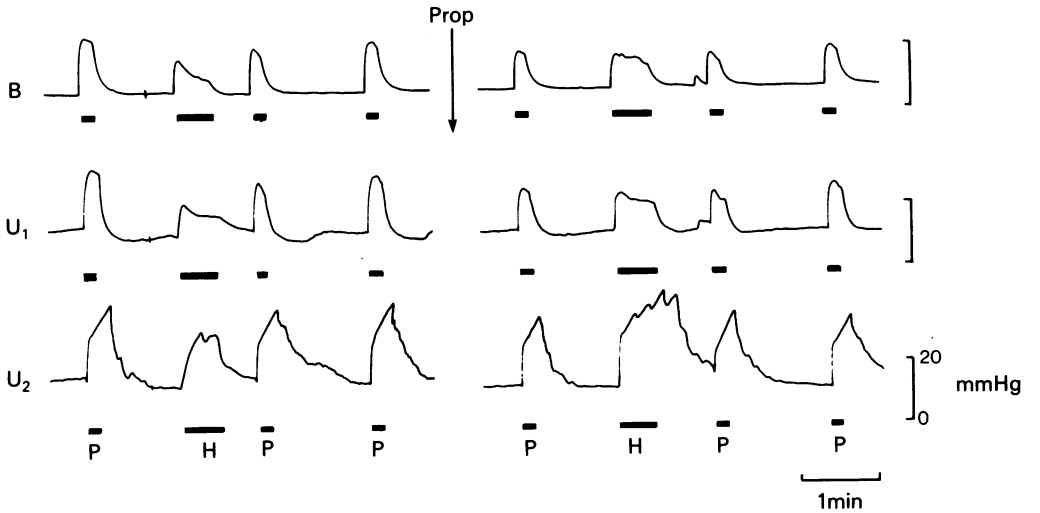

Figure 3 Stimulation of the hypogastric nerve (H) for 30 s slightly reduced the responses of both bladder and urethra to stimulation of the pelvic nerve (P) for 10 s. Propranolol (Prop, 0.05 mg/kg body wt.) prevented this reduction. In the presence of propranolol the bladder response to hypogastric nerve stimulation was better maintained and the urethral responses were increased.

resulted in a slightly delayed decrease in pressure (Figure 2). However, close arterial injection of any of these drugs caused only a slight bladder contraction and in many animals no response was seen. Following injection of isoprenaline the responses of U_1 to drugs and nerve stimulation tended to be similar to those of the bladder (B) whereas after phenylephrine the responses for the two parts of the urethra (U_1 and U_2) resembled each other and differed from the bladder response. This suggests that the β-adrenoceptor action of noradrenaline relaxed the bladder neck and the α-adrenoceptor action constricted it.

The effects of antagonists

The effects of adrenoceptor blocking agents and other antagonists on the response to hypogastric nerve stimulation were investigated. In all animals the α-adrenoceptor antagonist, phentolamine, (1 to 2 mg/kg body wt.) significantly reduced the contractile responses of the bladder and of the urethra (Table 1) (Figure 1). The bladder response was never completely abolished but the urethral response was often reduced to zero and in 2 animals nerve stimulation in the presence of phentolamine relaxed the urethra. The β-adrenoceptor antagonist propranolol (0.05 to 0.2 mg/kg body wt.) was without significant action in the bladder but usually increased the initial contraction of the urethra (Table 1). In the presence of this drug the pressure increase of the bladder tended to be better maintained during the period of stimulation (Figure 3).

Of the other antagonist drugs used, atropine (0.05 to 0.1 mg/kg body wt.) and hexamethonium (1 to 2 mg/kg body wt.) had no significant effect on the contractile responses of either urethra or bladder to hypogastric nerve stimulation (Table 1). These doses maximally reduced responses to pelvic nerve stimulation or to close arterial injection of acetylcholine in the same animals (Creed & Tulloch, 1978). Methysergide (0.04 to 0.1 mg/kg body wt.) was also without effect on the hypogastric nerve response and failed to block the contractile response to 5-hydroxytryptamine. Quinidine (7 to 13 mg/kg body wt.) caused reduction in the contraction of both the bladder and urethra to hypogastric nerve stimulation (Figure 1) but also to pelvic nerve stimulation and may be producing a general decrease in excitability rather than specifically blocking the action of adenosine triphosphate (ATP), a possible transmitter (Burnstock, Dumsday & Smythe, 1972).

Interaction with acetylcholine or pelvic nerve responses

Hypogastric nerve stimulation. Stimulation of the pelvic nerve on one side for periods of 30 s produced increases in pressure of both the urethra and the bladder which were maintained throughout the period of stimulation. Supramaximal stimulation of the hypogastric nerves for 10 s in the middle of such a period did not alter the responses to pelvic nerve stimulation when this was either supramaximal or submaximal (Figure 4). On the other hand, if the pelvic nerve was stimulated during a long period of hypogastric stimu-

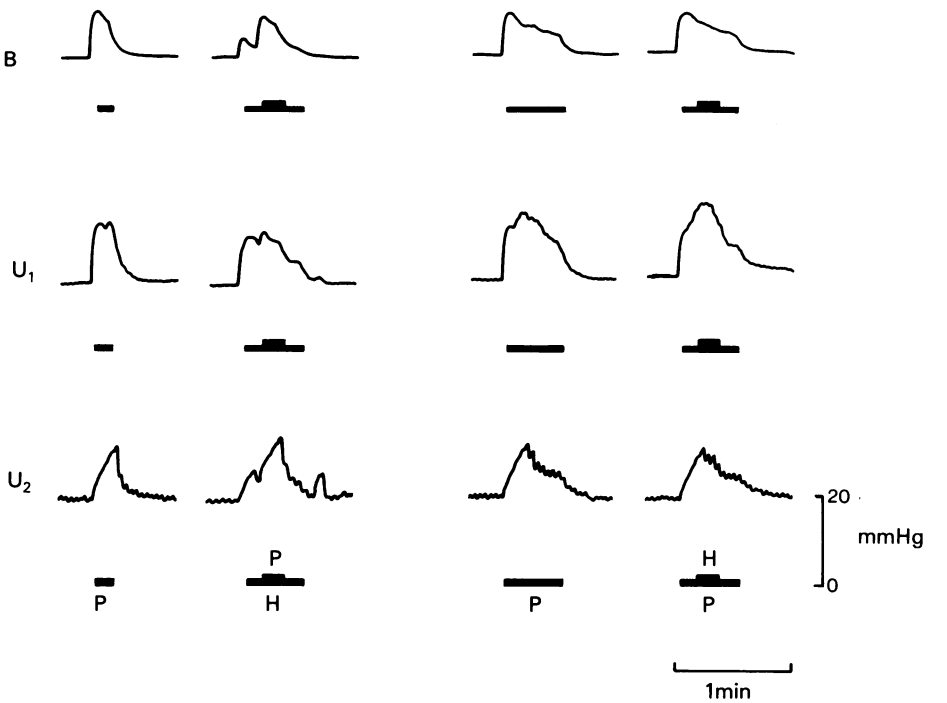

Figure 4 Interaction between supramaximal responses to pelvic (P) and hypogastric (H) nerve stimulation (10 Hz, 16 V). The bladder response produced by pelvic nerve stimulation for 10 s was smaller during hypogastric nerve stimulation. However, hypogastric nerve stimulation for 10 s during prolonged pelvic nerve stimulation (30 s) was without effect.

lation the responses were reduced compared with those produced by pelvic nerve stimulation alone (Figure 4). This inhibition by the hypogastric nerve only occurred with long periods of stimulation (over 30 s) and lasted for several minutes after the end of stimulation. Comparison of responses to pelvic nerve stimulation before and after hypogastric stimulation (Figure 3) indicated that the reduction was significant (Table 2). The responses of the bladder to close arterial injection of acetylcholine (50 to 100 μg) were not significantly reduced by hypogastric nerve stimulation, but the reduction of the urethra was significant at the 5% level.

In the presence of propranolol (0.1 to 0.2 mg/kg

Table 2 The effect of drugs and hypogastric nerve stimulation on subsequent responses of bladder and urethra

	Urethra				*Bladder*			
	Control (mmHg)	*After drug or H (mmHg)*	P	n	*Control (mmHg)*	*After drug or H (mmHg)*	P	n
PS PhE	18.0 ± 10.2	19.2 ± 9.2	NS	4	17.1 ± 7.2	19.0 ± 6.4	*	10
PS Isop	19.3 ± 5.9	14.8 ± 5.2	***	28	15.7 ± 5.4	10.9 ± 4.3	***	16
PS 5-HT	16.2 ± 8.1	23.2 ± 13.1	**	31	15.4 ± 6.8	22.6 ± 8.2	**	17
PS H	17.4 ± 6.2	14.0 ± 7.6	***	34	15.9 ± 5.3	11.3 ± 5.5	***	16
ACh Isop	8.5 ± 5.2	5.7 ± 3.8	**	22	7.6 ± 6.1	3.5 ± 3.3	**	11
ACh 5-HT	6.8 ± 5.3	7.3 ± 5.5	NS	12	6.2 ± 6.0	5.6 ± 3.6	NS	5
ACh H	10.3 ± 6.0	7.7 ± 4.9	*	14	8.1 ± 4.5	6.4 ± 3.9	NS	11

The pressure increase produced in response to pelvic nerve stimulation (PS) or to acetylcholine (ACh) were recorded before and after treatment with phenylephrine (PhE), isoprenaline (Isop) or 5-hydroxytryptamine (5-HT) or hypogastric nerve stimulation (H). Details as in Table 1.

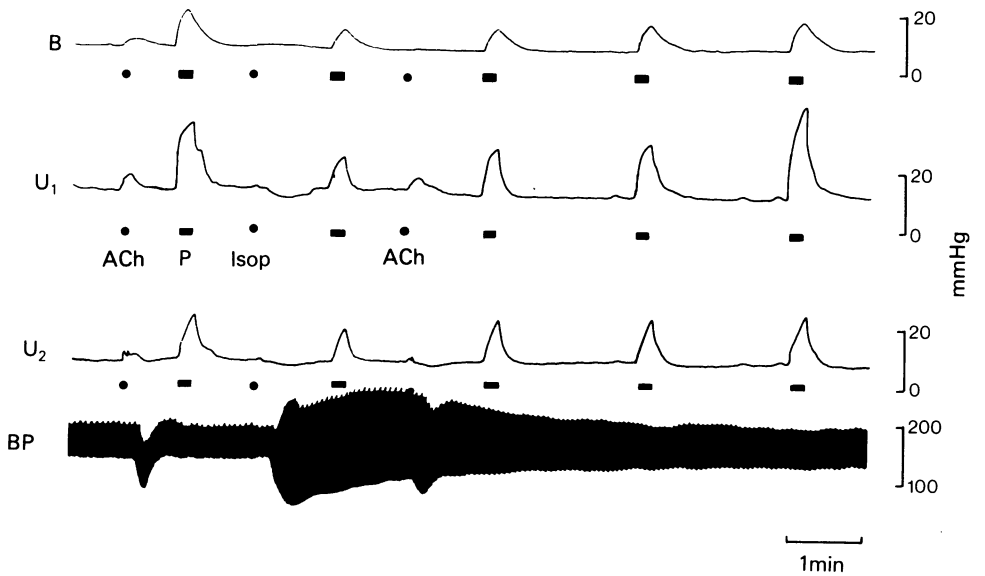

Figure 5 The effect of isoprenaline (Isop, 30 μg) on the responses to pelvic nerve stimulation (P and at each bar) and close arterial injection of acetylcholine (ACh, 50 μg). Isoprenaline reduced all responses of both bladder and urethra and this inhibition lasted several minutes. This dose of isoprenaline increased systemic blood pressure and pulse pressure (BP).

body wt.) some inhibition of the pelvic responses still occurred but it was smaller and did not last as long (Figure 3). Phentolamine (1 to 2 mg/kg body wt.) was without effect, suggesting that it is only the β-adrenoceptor action of noradrenaline that is involved. The ganglion blocking agent, hexamethonium, (1 to 2 mg/kg body wt.) reduced the responses to pelvic nerve stimulation and the remaining responses were no longer inhibited by hypogastric nerve stimulation.

Biogenic amines. Close arterial injection of phenylephrine (10 to 30 μg) produced a prolonged increase in the pressure of the urethra so that in most animals it was not possible to compare accurately the responses to pelvic nerve stimulation before administration, with those afterwards. However, in the bladder the increase was transient and the pressure normally returned to the original baseline within 30 s. The slight increase in response to pelvic nerve stimulation in the presence of phenylephrine was significant $P < 0.05$ (Table 2). There was a highly significant increase in the responses to hypogastric nerve stimulation in the presence of phenylephrine (3.6 to 4.5 mmHg; $n = 14$, $P = <0.001$).

Isoprenaline (10 to 30 μg) relaxed the bladder and urethra and significantly reduced the responses of both to pelvic nerve stimulation and to close arterial injection of acetylcholine (Table 2) (Figure 5). The inhibition occurred within one minute and lasted for up to 15 min. Propranolol reduced the inhibition produced by isoprenaline. In the presence of hexamethonium, isoprenaline still inhibited the responses to pelvic nerve stimulation and to acetylcholine (Figure 6) suggesting that the isoprenaline acts at least in part directly on the smooth muscle.

5-Hydroxytryptamine (20 to 50 μg) produced an increase in bladder and urethral pressures without significantly affecting the blood pressure (Figure 7). In addition it enhanced the responses to both pelvic nerve stimulation and close arterial injection of acetylcholine (Table 2). This enhancement lasted for up to 15 min and was not affected by propranolol, methysergide or phentolamine. In the presence of hexamethonium, 5-hydroxytryptamine produced only a slight increase in pressure and no longer altered the responses to pelvic nerve stimulation.

Discussion

The responses of both bladder and urethra to stimulation of the hypogastric nerves were reduced by phentolamine and slightly enhanced or prolonged by propranolol suggesting that there are adrenergic fibres with α excitatory action and β inhibitory action. Close arterial injection of agonist drugs supported this for the urethra since the α-adrenoceptor agonist, phenylephrine, increased the urethral pressure and the β-adrenoceptor agonist, isoprenaline, decreased it. However, in the bladder close arterial injection of

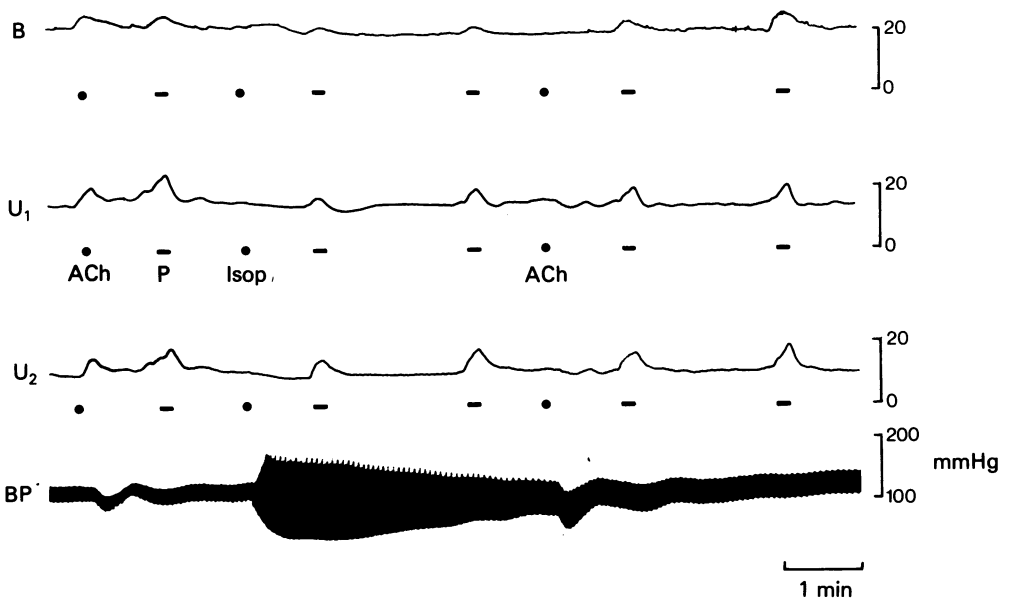

Figure 6 In the presence of hexamethonium (2 mg/kg body wt.) isoprenaline (Isop, 30 μg) still reduced the responses to pelvic nerve stimulation and to acetylcholine (ACh, 50 μg). Hexamethonium itself greatly reduced the responses to pelvic nerve stimulation (these results and those in Figure 5 are from the same animal).

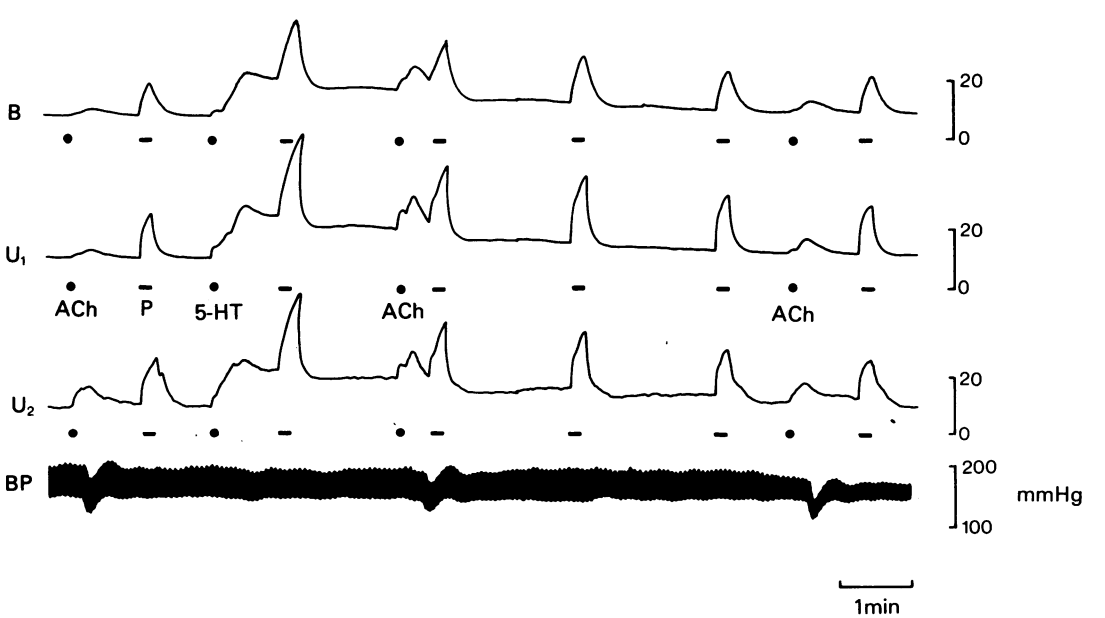

Figure 7 The effect of 5-hydroxytryptamine (5-HT, 50 μg) on responses to pelvic nerve stimulation and to acetylcholine (ACh, 50 μg). All responses were enhanced for several minutes. There was a small effect on blood pressure.

either drug was usually without effect. Sympathomimetic drugs are usually without action on strips of bladder from several species including guinea-pig (Dave & Dhattiwala, 1976) and human (Awad *et al.*, 1974) as well as dog (Creed, unpublished). This indicates that the negative response to close arterial injection was not due to poor accessibility produced by local vasoconstriction, and therefore, direct innervation is unlikely to involve adrenergic fibres.

The inhibitory action of phentolamine could alternatively be due to its action on other receptor sites. Atropine, hexamethonium and methysergide did not significantly alter the responses to hypogastric nerve stimulation suggesting that the receptors for acetylcholine and 5-hydroxytryptamine are probably not important. Furthermore, phentolamine does not block the contractile responses of bladder strips to histamine (Khanna, de Gregorio, Sample & McMichael, 1977) or 5-hydroxytryptamine (Saum & de Groat, 1973). Receptors to other possible transmitters have not been tested.

Thirdly, an inhibitory action of phentolamine would be seen if the adrenergic transmitter, noradrenaline, were to enhance other pathways activated at the same time by hypogastric nerve stimulation. This is supported by the observation that phenylephrine significantly increased the response of the bladder to hypogastric nerve stimulation. The smooth muscle of the bladder has a sparse adrenergic innervation but many fibres end on ganglion cells in the bladder wall (Hamberger & Norberg, 1965; Gosling & Dixon, 1975). The released noradrenaline may therefore act on these ganglia. Although hexamethonium did not significantly reduce the responses of the bladder to hypogastric nerve stimulation suggesting that there may be no cholinergic ganglionic relay, excitatory postsynaptic potentials have been recorded from pelvic ganglion cells following hypogastric nerve stimulation of the guinea-pig (McLachlan, 1977).

There is already some evidence that hypogastric nerve stimulation modifies the responses of the bladder to pelvic nerve stimulation. In the cat, electrical stimulation of the hypogastric nerves produced direct depression of transmission in vesical parasympathetic ganglia since the postganglionic action potentials were reduced (de Groat & Saum, 1972). This effect was mediated via α-adrenoceptors. In addition there was direct depression of smooth muscle cells via β-adrenoceptors. An inhibitory action by isoprenaline has also been recorded in man (Hindmarsh, 1977). In the present experiments phenylephrine produced an insignificant increase in responses to pelvic nerve stimulation but these responses and those to acetylcholine were reduced significantly by isoprenaline. Since some reduction to isoprenaline still occurred in the presence of hexamethonium, at least some of the β action is probably directly on the smooth muscle. On the other hand the inhibitory effect of hypogastric nerve stimulation was greatly reduced by hexamethonium and had relatively little effect on the response to acetylcholine which acts mainly on the smooth muscle (Creed & Tulloch, 1978). The noradrenaline released from the nerves may therefore act almost entirely on the ganglia where most of the adrenergic fibres end.

The smooth muscle cells of the urethra have a much more dense adrenergic innervation than the bladder (Gosling & Dixon, 1975) and associated with this hypogastric nerve stimulation or injection of noradrenaline has a much larger direct action on the urethra. In addition the present experiments suggest that the hypogastric nerves also modify inputs to the urethra since the effects of stimulation or catecholamines on the responses of the urethra to pelvic nerve stimulation are parallel to those of the bladder.

Apart from noradrenaline there is now some evidence that 5-hydroxytryptamine may also modify transmission through the pelvic plexus. This agent produces a biphasic increase in bladder pressure which has been reported to be due to direct action on smooth muscle, blocked by methysergide, and indirect stimulation of the pelvic ganglion cells (Gyermek, 1962). In addition it potentiates responses to pelvic nerve stimulation or to acetylcholine (Gyermek, 1962; Hindmarsh *et al.*, 1977). In the present experiments the responses of the urethra were also enhanced. The potentiation was not blocked by methysergide but no longer occurred in the presence of hexamethonium suggesting that 5-hydroxytryptamine is acting on the ganglia. There was no evidence of initial depression as reported by Saum & de Groat (1973).

The results therefore suggest that there is direct adrenergic innervation of the urethra but bladder adrenergic innervation is sparse. However, non-adrenergic fibres in the hypogastric nerve probably cause direct bladder contraction. Hypogastric nerves also modify inputs to both bladder and urethra probably by acting on the ganglia in the pelvic plexus. This effect is inhibitory via β-adrenoceptors, but may also be excitatory via α-adrenoceptors or tryptaminergic receptors. The results give no indication of the nature of the non-adrenergic fibres in the hypogastric nerves.

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References

ALM, P. & ELMER M. (1975). Adrenergic and cholinergic innervation of the rat urinary bladder. *Acta physiol. scand.*, **94**, 36–45.

AWAD, S.A., BRUCE, A.W., CARRO-CIAMPI, G., DOWNIE, J.W., LIN, M. & MARKS, G.S. (1974). Distribution of α- and β-adrenoceptors in human urinary bladder. *Br. J. Pharmac.*, **50**, 525–529.

BURNSTOCK, G., DUMSDAY, B. & SMYTHE, A. (1972). Atropine resistant excitation of the urinary bladder: the possibility of transmission via nerves releasing a purine nucleotide. *Br. J. Pharmac.*, **44**, 451–461.

CREED, K.E. & TULLOCH, A.G.S. (1978). The effect of pelvic nerve stimulation and some drugs on the urethra and bladder of the dog. *Br. J. Urol.*, (in press).

DAVE, K.C. & DHATTIWALA, A.S. (1976). Adrenoceptors of the guinea pig urinary bladder. *Br. J. Pharmac.*, **58**, 37–41.

DE GROAT, W.C. & SAUM, W.R. (1972). Sympathetic inhibition of the urinary bladder and of pelvic ganglionic transmission in the cat. *J. Physiol.*, **220**, 297–314.

EDVARDSEN, P. & SETEKLEIV, J. (1968). Distribution of adrenergic receptors in the urinary bladder of cats, rabbits and guinea pigs. *Acta pharmac. tox.*, **26**, 437–445.

ELLIOTT, T.E. (1907). The innervation of the bladder and urethra. *J. Physiol.*, **35**, 367–445.

GOSLING, J.A. & DIXON, J.S. (1975). The structure and innervation of smooth muscle in the wall of the bladder neck and proximal urethra. *Br. J. Urol.*, **47**, 549–558.

GYERMEK, L. (1962). Action of 5-hydroxytryptamine on the urinary bladder of the dog. *Archs int. Pharmacodyn.*, **137**, 137–144.

HAMBERGER, B. & NORBERG, K-A. (1965). Studies on some systems of adrenergic synaptic terminals in the abdominal ganglia of the cat. *Acta physiol. scand.*, **65**, 235–242.

HINDMARSH, J.R., IDOWU, O.A., YEATES, W.K. & ZAR, M.A. (1977). Pharmacology of electrically evoked contractions of human bladder. *Br. J. Pharmac.*, **61**, 115P.

KHANNA, O.P., DE GREGORIO, G.J., SAMPLE, R.G. & MCMICHAEL, R.D. (1977). Histamine receptors in urethrovescal smooth muscle. *Urology*, **10**, 375–381.

MANTEGAZZA, P. & NAIMZADA, K.M. (1967). Observations on an isolated preparation of guinea-pig urinary bladder stimulated through the hypogastric nerves. *Eur. J. Pharmac.*, **1**, 396–401.

MCLACHLAN, E.M. (1977). Interaction between sympathetic and parasympathetic pathways in the pelvic plexus of the guinea pig. *Proc. Aust. Physiol. Pharmac. Soc.*, **8**, 15P.

NERGÅRDH, A. & BORÉUS, L.O. (1972). Autonomic receptor function in the lower urinary tract of man and cat. *Scand. J. Urol. Nephrol.*, **6**, 32–36.

RAZ, S. & CAINE, M. (1972). Adrenergic receptors in the female canine urethra. *Invest. urol.*, **9**, 319–323.

SAUM, W.R. & DE GROAT, W.C. (1973). The actions of 5-hydroxytryptamine on the urinary bladder and on vesical autonomic ganglia in the cat. *J. Pharmac. exp. Ther.*, **185**, 70–83.

TAIRA, N. (1972). The autonomic pharmacology of the bladder. *A. Rev. Pharmac.*, **12**, 197–208.

TULLOCH, A.G.S. (1974). The vascular contribution to intraurethral pressure. *Br. J. Urol.*, **46**, 659–664.

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