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EVIDENCE FOR A DUAL PELVIC NERVE INFLUENCE ON LARGE BOWEL MOTILITY IN THE CAT

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SUMMARY

1. The effects of efferent electric pelvic nerve stimulation on colorectal motility and blood flow with emphasis on the motor responses in consecutive colonic and rectal segments were studied in anaesthetized cats. It was considered of particular interest to explore whether selective pharmacological blockade and graded nerve stimulations might reveal the presence of functionally differentiated efferent fibres controlling colonic motility.

2. Pelvic nerve stimulation induced immediate and sustained colorectal contractions and a simultaneous increase of the over-all colonic blood flow. The excitatory responses declined immediately on cessation of a shortlasting stimulation (< 2 min); after a longlasting one, however, the rectal contraction was maintained for several min.

3. The colonic contraction on pelvic nerve stimulation remained unchanged after atropine but was delayed in onset. Moreover, in the transverse and distal colon it was preceded by a relaxation which was most pronounced in the distal part. The vasodilator response was unchanged.

4. After atropine the rectal segment showed a purely relaxatory response. Despite continuous pelvic nerve stimulation the relaxation vanished, however, and rectal volume returned to resting level with 3–5 min. On cessation of such a prolonged stimulation there was a marked rectal 'after-contraction'.

5. The excitation thresholds for the efferent nerve fibres eliciting these different responses could not be separated. The motility and the vasodilator responses were not influenced by adrenergic or by serotoninergic blockade.

6. The results indicate that direct preganglionic stimulation of the cat pelvic nerves activates intramural cholinergic excitatory neurones as well as non-cholinergic excitatory neurones and furthermore, non-adrenergic non-cholinergic inhibitory neurones, which together result in most complex colonic and rectal motor responses. From a functional point of view these centrally controlled responses may well be independently controlled by separate preganglionic neurones though they do not differ concerning excitation thresholds.

7. The effects are consistent with a dual function of the distal colon and rectum. Such a dual parasympathetic influence on the large bowel simulates the vagal control of the stomach, where specific vagal relaxatory fibres convey a reflex widening of the corpus-fundus reservoir during food intake.

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INTRODUCTION

Efferent electric stimulation or reflex activation of the parasympathetic pelvic nerves cause sustained colonic contraction and these nerves are most important for the expulsive function of the large bowel. The contraction, which involves the entire colon, is generally considered to be non-cholinergic although it is sometimes modestly reduced by atropine (Langley & Andersson, 1895; Füllgraff & Schmidt, 1963; Füllgraff, Schmidt & Azokwu, 1964, Hultén, 1969; Goldenburg & Burns, 1971). The transmitter(s) responsible for the non-cholinergic contraction is not known. There is also an associated mucous secretion and vasodilatation but only the secretory response appears to be abolished by atropine (Hultén, 1969).

Storage is another important function exhibited by the colon, both in animals and man. Although pelvically induced colonic motility can be markedly damped by activation of the adrenergic lumbar colonic nerves, exerting their inhibitory influence on intramural synapses (Learmonth & Markowitz, 1930; Hultén, 1969), there is no evidence that these nerves are specifically involved in the control of storage function.

Non-adrenergic, non-cholinergic inhibitory neurones have been demonstrated in the intrinsic nervous system throughout the gut, (Burnstock, 1972; Furness & Costa, 1973). In the stomach these inhibitory neurones are centrally controlled by specific vagal nerve fibres which appear to be responsible for the gastric receptive relaxation (Martinson, 1965; Jansson, 1969; Abrahamsson, 1973). Whether a similar integrated nervous regulation for appropriate adjustment of the colonic motility is exerted by the pelvic nerves is unknown.

The aim of the present investigation was to study in more detail the effects of pelvic nerve stimulation on colonic motility and blood flow with emphasis on the motor responses in consecutive colonic and rectal segments. Particular interest was devoted to the question whether selective pharmacological blockade and graded nerve stimulations might reveal the presence of functionally differentiated efferent fibres controlling colonic motility.

METHODS

Operative procedures. Thirty cats, fasted for 24 h were anaesthetized intravenously with chloralose (50–70 mg/kg) after induction with ether. A tracheal cannula was inserted to allow a free airway. The arterial pressure was recorded from a femoral artery by means of a Statham pressure transducer (P 23 AC). The abdomen was opened in the mid-line and the greater omentum, the spleen and the small intestine were extirpated. In order to prevent adrenal secretion from interfering with the effects on intestinal smooth muscles the adrenals were excluded from the circulation by encircling ligatures in some experiments. The contents of the colon were removed by rinsing with saline prior to recording of motility. After surgery the cats were heparinized (300 i.u./kg).

Recording of motility. Colonic motility was studied by a volume recording device. One flaccid rubber balloon about 2 cm long and wide enough to prevent complete expansion at maximal intestinal relaxation was introduced via the anus and placed in the segment just oral to the levator muscles but still below the sacral promontory. This segment will be referred to as the rectum, the upper limit of which corresponds to the level where the descending branch of the inferior mesenteric artery pierces the intestinal wall. The position of this balloon could be changed deliberately during the course of the experiments and placed in the segment just cranial to the sacral promontory, referred to as the distal colon (Fig. 1). Another balloon of a similar

dimension was introduced into the colon through a small incision in the caecum for recording of motility in the most oral part of the colon (proximal colon) but could be moved for recording of transverse colonic motility. The balloons were connected to water reservoirs by means of wide bore rubber tubings and the systems were filled with body-warm water. The water reservoirs were suspended in weight recorders (Grass Force Displacement Transducer FT 10 C) operating a Grass Polygraph, model 7 D. The pressure was usually set at 15 cmH_2O. Due to the wide dimensions of the reservoirs the pressure could be kept constant despite variations in volume.

To exclude reflex interference from the anal region, in three experiments the rectum was divided beneath the entrance of the pelvic plexus at the level of the levator muscles. In these experiments the rectal balloon was introduced into the rectum via its distal cut end. In four experiments the effects of pelvic nerve stimulation on intraluminal pressure at different levels of the colon–rectum were also recorded by means of a pressure sensitive catheter (Gaeltec 6092) introduced via the anal canal.

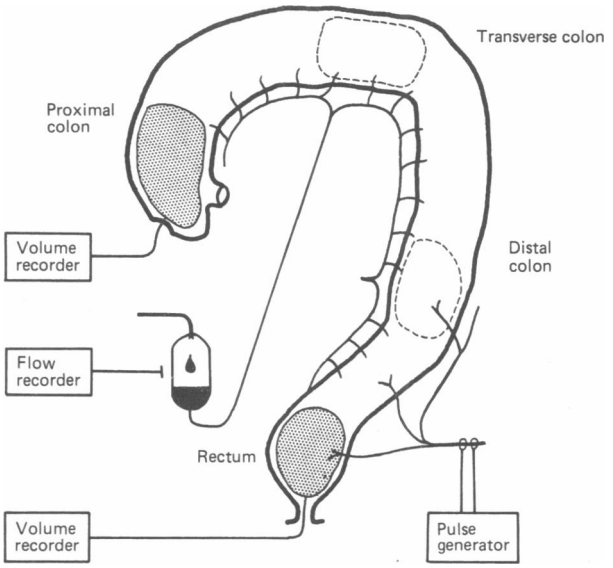

Fig. 1. Schematic illustration of the preparation.

Recording of colonic blood flow. To determine the magnitude of the over-all colonic blood flow the superior mesenteric arterial inflow of the colon was recorded. The inferior mesenteric artery therefore had to be divided. It has been shown that this procedure does not change total colonic blood flow, not even during maximal flow levels (Hultén, 1969). A wide bore polyethylene tube was inserted into a carotid artery and the blood flow diverted to a closed Perspex optical drop chamber filled with silicone oil, and connected to the proximal end of the centrally cut superior mesenteric artery. An optical drop counter operated an ordinate writer which recorded flow rate on the polygraph (Fig. 1).

Nervous stimulation. All periarterial nervous tissue along the superior and inferior mesenteric arteries was divided. The pelvic nerves on both sides were dissected free, divided as they emerged from the sacral roots and their peripheral ends mounted on silver ring electrodes for subsequent efferent electrical stimulation. Supramaximal square wave pulses were delivered from a Grass stimulator, model S 5E. The stimulation frequency was set to 5 Hz, which corresponds to the upper range of physiological discharge rates. If not otherwise stated the pulse duration was kept at 5 msec. The voltate was 8 V.

Administration of drugs. Phentolamine (Regitine; reagent grade, Ciba) 10 mg/kg, I.V. and propranolol chloride (Inderal, reagent grade, ICI-Pharma) 3 mg/kg, I.V. were used as α- and β-blocking agents respectively. The blocking effects were tested by close I.A. injections of noradrenaline and isoprenaline. Dihydroergotamine (DHE; Orstanorm; reagent grade, Sandoz), a serotonin blocking agent, was given as bolus injection in the colonic vascular bed while occluding

the superior mesenteric artery (Biber, 1973). The effect of the blockade was tested by I.A. infusion of serotonin (Serotonin creatinine sulphate, Sigma Chemical Co.). Atropine sulphate was administered I.V. Hexamethonium (Hexamethonium bromide, SIGMA) was used as ganglionic blocking agent and infused at a rate of 100 μg/kg per min, I.V., to a dose of 400 μg/kg.

RESULTS

'Resting' colonic motility and blood flow. The volume changes of proximal and transverse colon where characterized by slow but significant volume reductions lasting for 10–40 sec. and occurring with a frequency of 0·5–1/min. The rhythmic activity in the distal colon was slower and volume changes occurred less frequently. The rectum usually showed no volume changes at all.

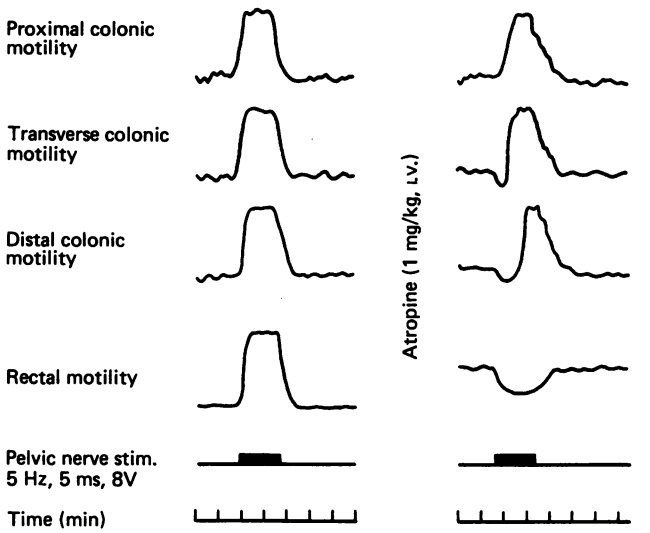

Fig. 2. Effects of pelvic nerve stimulation on consecutive colonic and rectal segments before (left panel) and after (right panel) atropine. Note that the colonic contraction is somewhat delayed after atropine and that in the transverse and distal colonic segments it is preceded by a transient relaxation, while the rectal segment shows a purely relaxatory response.

Atropine treatment (0·1–10 mg/kg, I.V.) almost completely abolished spontaneous motility in the colon and also lowered the resting tone, as reflected by a volume increase. In contrast, increased rectal tone was regularly observed after atropine, and superimposed contractions occurring with a frequency of 1–2/min were often seen.

Resting colonic blood flow amounted to about 20 ml./min per 100 g tissue and did not change after atropine treatment. Only when intense, the spontaneous motility caused synchronous minor changes in blood flow.

Effects of shortlasting supramaximal pelvic nerve stimulation. As is shown in the left panel of Fig. 2, shortlasting (i.e. < 2 min) efferent stimulation of the pelvic nerves produced a powerful colonic contraction, which appeared within 5 sec and which was well maintained throughout the stimulation both in the colon and the rectum.

After cessation of stimulation the motor response declined within 30 sec in all parts of the colon including the rectum.

Atropine treatment (0·1–10 mg/kg) which eliminated spontaneous colonic motility, changed the motor response to pelvic nerve stimulation in the different parts of the colon in a characteristic pattern. Thus, in the proximal colon the motor contraction,

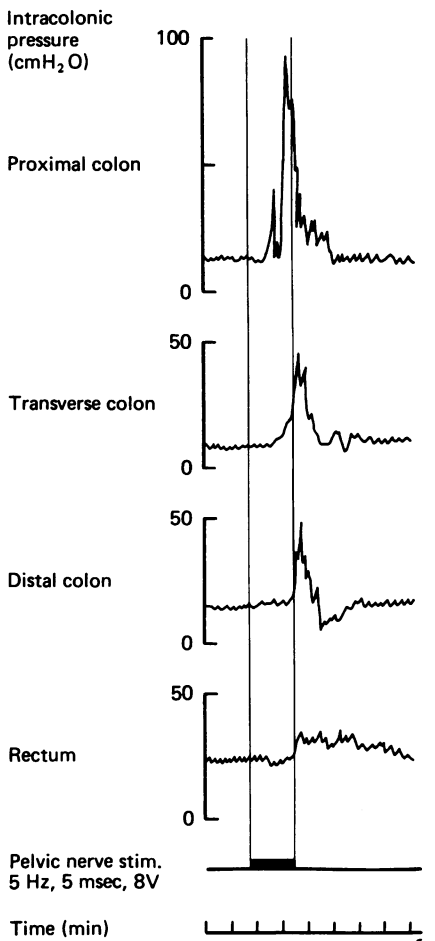

Fig. 3. Effects of pelvic nerve stimulation on the intraluminal pressure in consecutive colonic and rectal segments after atropine. Note the delayed pressure increase in the colonic segments and the absence of pressure reductions.

which was unchanged in magnitude, did not appear until 30–40 sec after commencement of the stimulation. Also in the transverse and distal colon the magnitude of contraction was unchanged but it was preceded here by an immediate and transient relaxation, which was regularly more prolonged in the distal colon (Fig. 2, right panel). A prominent relaxation was regularly observed in the rectum after atropine treatment and it was here regularly well maintained throughout the stimulations. After cessation of stimulation 'resting' tone was regained within 1 min (Fig. 2, right panel). Exclusion of the adrenals from the circulation or severing the rectum

at the level of the levator muscles, excluding any influences from the anal region, did not change the response. When instead studied by means of intraluminal pressure-sensitive catheters, marked pressure increases were recorded in the colon about 30–60 sec after commencement of the stimulation and reductions of intraluminal pressure were not observed either in the colon or in the rectum (Fig. 3).

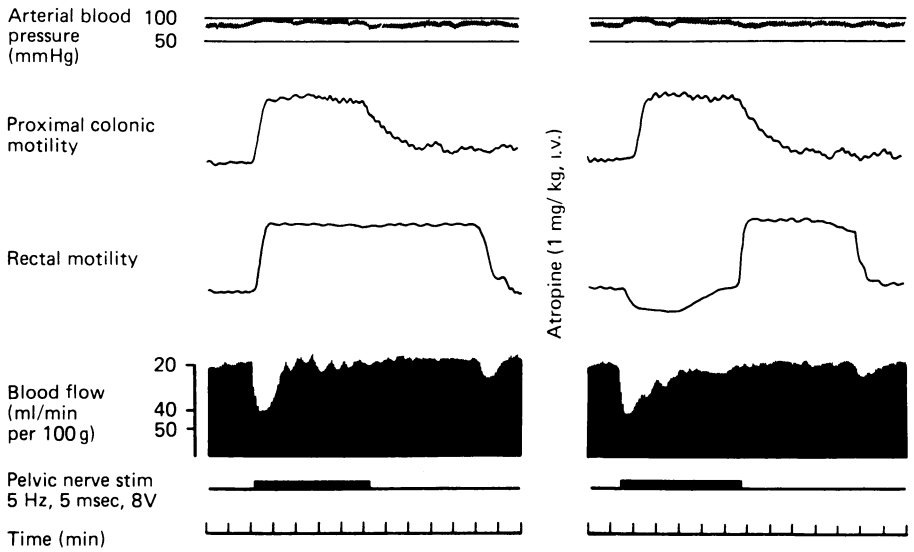

Fig. 4. Effects of prolonged pelvic nerve stimulation on proximal and rectal motility and total colonic blood flow before (left panel) and after atropine (right panel). Note that the sustained rectal contraction is reversed into a relaxation after atropine, and that a marked rectal 'rebound' contraction ensues upon cessation of stimulation.

Pelvic nerve stimulation increased total colonic blood flow within 5–10 sec after commencement of the stimulation. The transient blood flow increase, which reached peak level within 20–30 sec was not delayed by atropine but in some experiments the duration of the blood flow increase was prolonged and sometimes even outlasted the stimulation period.

Effects of prolonged pelvic nerve stimulation (3–10 min). The magnitude of excitatory responses to pelvic nerve stimulation was well maintained in all parts of colon and in the rectum, even during prolonged stimulation. On cessation of such stimulations the excitatory colonic responses declined immediately to reach control within 1–2 min, while the rectal ones were maintained for minutes after cessation of the stimulation (Fig. 4).

After atropine (1 mg/kg, I.V.) colonic responses to prolonged pelvic nerve stimulation were similar to these during shortlasting stimulation. However, the rectal relaxatory responses after atropine subsided during stimulation, and within 3–5 min the volume had returned to control despite continuous stimulation, as is shown in Fig. 4. Furthermore, there was an immediate and marked contraction after cessation of stimulation. This 'after-contraction' was maintained for 2–6 min but was promptly reversed to a relaxation on recommencement of the stimulation. The pattern of response did not change during the course of the experiments.

As seen in Fig. 4, the initial blood flow increase was sometimes more longlasting after atropine, particularly during the first 2–3 min when the rectal relaxation was still maintained. On repetition of a supramaximal stimulation the magnitude of the increase in the blood flow shortly after a prolonged stimulation was unchanged.

Effects of graded pelvic nerve stimulation on colonic blood flow and motility. In attempts to determine the stimulation thresholds of nerve fibres mediating colonic motility and vasomotor effects, the pulse duration was varied over a wide range, while frequency and voltage were kept constant at 5 Hz and 8 V, respectively. A clear-cut colorectal contraction and a vasodilatation appeared with a pulse duration of 0·1 msec. Maximal responses, with respect to both volume reduction and blood flow increase, were obtained at 0·5 msec. Increasing the pulse duration over a wide range did not provide evidence for the existence of efferent pelvic nerve fibres to the muscle coat and blood vessels, which differed concerning neurophysiological properties. After atropine, the threshold for evoking vasodilator responses and colonic contractions was unchanged. Also the rectal relaxation appeared at pulses of 0·1 msec duration with maximal responses at 0·5 msec.

Effects of pharmacological receptor blockade and ganglionic blocking agents. Administration of phentolamine (10 mg/kg, I.V.) and propranolol (3 mg/kg, I.V.), doses which completely abolished effects of noradrenaline and isoprenaline, did not change the responses to pelvic nerve stimulation whether before or after atropine. Thus, the distal colonic and rectal relaxations, elicited by pelvic nerve stimulation after atropine, do not appear to be mediated by adrenergic mechanisms. Dihydroergotamine, considered to have serotonin receptor blocking properties, had no influence on either the vasodilator or motility responses. The adequacy of this blockade was checked by close intra-arterial infusion of serotonin (50 μg/min per 100 g colonic tissue). Hexamethonium (400 μg/kg, I.V.) completely abolished the vasodilator response as well as the contraction and the relaxation on pelvic nerve stimulation, suggesting that these effects were all mediated by intramural post-ganglionic neurones.

DISCUSSION

The present results suggest that the pelvic nerves influence colorectal motility and blood flow by different modes of action. Thus, motility is modulated in a differentiated fashion along the consecutive parts of the large intestine. Besides vasodilatation, pelvic nerve stimulation elicited tonic contractions in all colonic parts and the rectum, confirming most previous studies on the subject.

However, after atropine treatment the motor response to pelvic nerve stimulation changed markedly. Thus, although the proximal colon still exhibited tonic contractions similar to those prior to atropine treatment, a transient decline in tone now preceded contraction in the distal parts. These 'inhibitory' responses were more marked and extended in time the more distal the recordings, and in the rectum they appeared as clear-cut relaxations. The associated vasodilatation remained largely unaffected by atropine. Although no differences in preganglionic fibre characteristics could be found with respect to excitation threshold upon direct electric stimulation, the post-ganglionic effects on the intestinal smooth muscles were readily separated by selective pharmacological blockade, revealing cholinergic and non-cholinergic

non-serotoninergic contraction responses as well as a non-adrenergic relaxation. The neurogenic vasodilatation, with stimulation thresholds similar to that eliciting motility effects, was non-cholinergic in accordance with previous experience (Hultén, 1969).

Intrinsic non-adrenergic inhibitory neurones have been demonstrated throughout the mammalian gut (Burnstock, Campbell, Bennet & Holman, 1963; Martinson, 1965; Campbell, 1966; Furness, 1969; Ambache & Zar, 1970; Costa & Furness, 1973; Ohga & Taneike, 1977), including man (Crema, del Tacca, Frigo & Lecchini, 1968; Rikimaru, Fukushi & Suzuki, 1971; Bennet & Stockley, 1975). It has, however, often been considered unlikely that such intramural colonic neurones should be centrally controlled at all by efferent fibres running in the pelvic nerves. It is on the other hand well known that both direct and reflex activations of the pelvic nerves relax the internal anal sphincter (Schuster, 1968; Garrett, Howard & Jones, 1974). The present results suggest that the central influence on intrinsic inhibitory neurones involves also the rectum and major distal parts of the colon. This centrally controlled non-adrenergic, non-cholinergic rectal relaxation elicited by pelvic nerve activation has not been demonstrated experimentally before, although electrophysiological evidence for activation of such inhibitory neurones has been presented recently (Gonella & Gardette, 1974).

The fact that atropine causes a delay of the colonic contraction on pelvic nerve stimulation makes it likely that the prompt contraction present before atropine is transmitted by acetylcholine and that non-cholinergic mechanisms contribute to the more delayed though sustained contraction. This is in accordance with *in vitro* studies on guinea-pig ileum, where transmural electric field stimulation of plexus-containing muscle strips activates both cholinergic and non-cholinergic excitatory motor neurones (Ambache & Freeman, 1968).

Other results concerning transmural activations of excitatory neurones in the proximal colon of the guinea-pig suggest that serotonin might be the transmitter of the non-cholinergic excitatory responses (Furness & Costa, 1973). In the present investigation, however, serotonin blockade by dihydroergotamine did not abolish the non-cholinergic contraction on pelvic nerve stimulation, making it unlikely that serotonin should mediate pelvic nerve induced colonic contractions in the cat. On the other hand, the local vasodilator reflexes caused by mechanical stimulation of the cat small intestinal mucosa (Biber, 1973) and of the cat colon (Fasth, Hultén, Lundgren & Nordgren, 1977) are abolished by serotonin blockade with dihydroergotamine, though the precise nervous arrangements and transmitter(s) involved are not yet known.

The rectal contraction to pelvic nerve stimulation appeared to be purely cholinergic. The relaxatory response that occurred after atropine treatment was, however, not sustained but subsided during prolonged stimulation. This might indicate an activation of non-cholinergic excitatory neurones, also explaining the considerable 'after-contraction' that regularly occurred after cessation of such stimulations. These after-contractions might, however, also reflect myogenic rebound phenomena which often seem to occur after activation of inhibitory neurones (Campbell, 1966; Furness, 1971; Stockley & Bennet, 1973). Both views fit well with the functional aspect of a facilitated expulsion of rectal contents when the centrally induced relaxation ceases.

The transmission involved in the neurogenic vasodilatation evidently differs from that causing the motor response because the vascular response was entirely unaffected by atropine. The question of the transmitter(s) is still unsolved but recent results suggest that a kinin mechanism might be involved (Fasth, Hultén, Johnson, Nordgren & Zeitlin, 1978).

The effect of pelvic nerve stimulation on the large intestine has been subjected to detailed studies over the years, but the results are contradictory (cf. Hultén, 1969). Based on *in vitro* experiments, Langley & Anderson (1895) and Bayliss & Starling (1900–1) suggested that pelvic nerve stimulation caused colonic contraction that was only partly affected by atropine, later repeatedly confirmed (Füllgraff & Schmidt, 1963; Goldenberg & Burns, 1971; Rostad, 1973). Also Hultén (1969) noted that the excitatory response was not reduced by atropine, but observed that the contraction then occurred first after some delay and was often preceded by a slight and transient decline in tone. Transient inhibitory responses preceding the contraction were also observed by Bayliss & Starling (1900–1) but were ascribed to a descending aboral inhibition. In contrast to these *in vivo* experiments, Garry & Gillespie (1955) showed in an *in vitro* study on the rabbit colon that the motility response to pelvic nerve stimulation could be completely abolished by atropine.

The divergent results often obtained in previous studies on colonic function can be explained partly by the fact that the techniques used had allowed for only semi-quantitative estimations of the *average* volume changes in the entire colon or its major parts, which might provide erroneous information. It can not be excluded therefore that regional difference with respect to excitatory or inhibitory responses might have been masked in such studies. Moreover, the use of intraluminal pressure recording devices has obvious shortcomings in this respect, since relaxatory responses are easily overlooked.

The multiple set of volume recordings used in the present study facilitated the analysis of the various links involved in the neurogenic control of consecutive colonic parts and the rectum. The results indicate that direct preganglionic stimulation of the cat pelvic nerves activates intramural cholinergic excitatory neurones as well as non-cholinergic excitatory neurones and furthermore, non-adrenergic, non-cholinergic inhibitory neurones, which together result in most complex colonic and rectal motility responses. From a functional point of view these centrally controlled responses may well be independantly controlled by separate preganglionic neurones though they do not differ concerning excitation threshold. Anyhow, the effects correlate well with a dual function of the distal colon and rectum.

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REFERENCES

Abrahamsson, H. (1973). Studies on the inhibitory nervous control of gastric motility. *Acta physiol. scand.* suppl. 390, 1–38.

Ambache, N. & Freeman, A. (1968). Atropine-resistant longitudinal muscle spasm due to excitation of non-cholinergic neurones in Auerbach's plexus. *J. Physiol.* **199**, 705–727.

Ambache, N. & Zar, M. A. (1970). An inhibitory action of histamine on the guinea-pig ileum. *Br. J. Pharmac.* **38**, 229–240.

BAYLISS, N. M. & STARLING, E. H. (1900–1901). The movements and the innervation of the large intestine. *J. Physiol.* **26**, 107–118.

BENNET, S. & STOCKLEY, H. (1975). The intrinsic innervation of the human alimentary tract and its relation to function. *Gut* **16**, 443–453.

BIBER, B. (1973). Vasodilator mechanisms in the small intestine. *Acta physiol. scand.* suppl. 401, 1–31.

BURNSTOCK, G. (1972). Purinergic nerves. *Pharmac. Rev.* **24**, 509–581.

BURNSTOCK, G., CAMPBELL, G., BENNET, M. & HOLMAN, M. (1963). Inhibition of the smooth muscle of *taenia coli*. *Nature, Lond.* **200**, 581–582.

CAMPBELL, G. (1966). Nerve-mediated excitation of the taenia of the guinea-pig caecum. *J. Physiol.* **185**, 148–159.

COSTA, M. & FURNESS, J. B. (1974). The innervation of the internal anal sphincter of the guinea-pig. In *Proc. of the 4th int. Symp. on Gastrointestinal Motility*, ed. DANIEL, E. E., pp. 681–690. Vancouver: Mitchell Press.

CREMA, A., DEL TACCA, M., FRIGO, G. M. & LECCHINI, S. (1968). Presence of a non-adrenergic inhibitory system in the human colon. *Gut.* **9**, 633–637.

FASTH, S., HULTÉN, L., LUNDGREN, O. & NORDGREN, S. (1977). Vascular responses to mechanical stimulation of the mucosa of the cat colon. *Acta physiol. scand.* **101**, 98–104.

FASTH, S., HULTÉN, L., JOHNSSON, J., NORDGREN, S. & ZEITLIN, J. (1978). Mobilization of colonic kallikrein following pelvic nerve stimulation in the atropinized cat. *J. Physiol.* **285**, 471–478.

FÜLLGRAFF, G. & SCHMIDT, L. (1963). Zur frage der humoral Verursachten, atropinresistente Kontraktion am Pelvicus-Colo-Präparat von Katzen. *Medna exp.* **9**, 378–384.

FÜLLGRAFF, G., SCHMIDT, L. & AZOKWU, PH. (1964). Über die atropinresistente Neuromusculäre Übertragung am Pelvicus-Colo-Präparat der Katze. *Archs int. Pharmacodyn. Thér.* **149**, 537–551.

FURNESS, J. B. (1969). The presence of inhibitory nerves in the colon after sympathetic denervation. *Eur. J. Pharmacol.* **6**, 349–352.

FURNESS, J. B. (1971). Secondary excitation of intestinal smooth muscle. *Br. J. Pharmac.* **41**, 213–226.

FURNESS, J. B. & COSTA, H. (1973). The nervous release and the action of substances which affect intestinal muscle through neither adrenoreceptors nor cholinoceptors. *Phil. Trans. R. Soc.* B **265**, 123–133.

GARRETT, J. R., HOWARD, E. R. & JONES, W. (1974). The internal anal sphincter in the cat. *J. Physiol.* **243**, 153–166.

GARRY, R. C. & GILLESPIE, J. S. (1955). The response of the musculature of the colon of the rabbit to stimulation, *in vitro*, of the parasympathetic and of the sympathetic outflows. *J. Physiol.* **128**, 557–576.

GOLDENBURG, M. & BURNS, R. (1971). Atropine-resistant spasm of the dog colon induced by intermittent pelvic nerve stimulation. *Life Sci. Oxford.* **10**, 591–600.

GONELLA, J. & GARDETTE, B. (1974). Etude électromyographique *in-vivo* de la command nerveuse extrinsique parasympathique du colon. *J. Physiol., Paris* **68**, 395–413.

HULTÉN, L. (1969). Extrinsic nervous control of colonic motility and blood flow. *Acta physiol. scand.* suppl. 335, 1–116.

JANSSON, G. (1969). Extrinsic nervous control of gastric motility. An experimental study in the cat. *Acta. physiol. scand.* suppl. 326, 1–35.

LANGLEY, J. N. & ANDERSON, H. K. (1895). On the innervation of the pelvic and adjoining viscera. *J. Physiol.* **18**, 67–105.

LEARMONTH, J. & MARKOWITZ, J. (1930). Studies on the innervation of the large bowel. II. *Am. J. Physiol.* **94**, 501–504.

MARTINSSON, J. (1965). Studies on the efferent vagal control of the stomach. *Acta physiol. scand.* suppl. 255, 1–24.

OHGA, S. & TANEIKE, T. (1977). Dissimilarity between the response to adenosine triphosphate or its related compounds and non-cholinergic inhibitory nerve stimulation in the longitudinal smooth muscle of pig stomach. *Br. J. Pharmac.* **60**, 221–231.

RIKIMARU, A., FUKUSHI, Y. & SUZUKI, T. (1971). Evidence for the presence of non-adrenergic inhibitor nerves in the human taenia coli. *Tohoku J. exp. Med.* **104**, 199–200.

ROSTAD, H. (1973). Colonic motility in the cat. II. Extrinsic nervous control. *Acta physiol. scand.* **89**, 91–103.

SCHUSTER, M. M. (1968). Motor action of rectum and anal sphincters in continence and defecation. In *Handbook of Physiology*. Section 6, vol. IV, ed. CODE, C. F. & HEIDEL, W., pp. 2121–2140. Washington D.C.: Am. Physiol. Soc.

STOCKLEY, H. & BENNET, A. (1974). The intrinsic innervation of human sigmoid colonic muscle. In *Proc. of the 4th int. Symp. on Gastrointestinal Motility*, ed. DANIEL, E. E., pp. 165–176. Vancouver: Mitchell Press.