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Cholinergic control of pacemaker initiating phase III of the migrating myoelectric complex in sheep

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ABSTRACT

To estimate the region from which phase III of the migrating myoelectric complex (MMC) originates and to establish the role of nicotinic and muscarinic receptors in the initiation of this phase, chronic experiments were performed in eight sheep with bipolar platinum electrodes attached to the antral and small intestinal wall. Myoelectric activity was recorded by means of a multichannel electroencephalograph before and after slow intravenous injections of cholinergic agonists and antagonists as well as erythromycin, an agonist to the hormone motilin.

MMC phases were identified according to the criteria proposed by Code and Marlett. A total of 263 MMC cycles was observed with a duration of 103±24 and 91±26 min in fasted and non-fasted animals, respectively. In fasted sheep, 8.7% of phases III MMC originated from the pyloric antrum, 50.5% from the duodenal bulb, 29.7% from the duodenum, 8.7% from the jejunum and 2.3% from the ileum. In non-fasted sheep these values were: 10.3, 31.3, 39.4, 15.5 and 3.5%, respectively. Neither cholinergic agonists nor erythromycin markedly changed the site of phase III MMC start. Following administration of anticholinergic drugs phase III MMC was not observed in the antrum. In fasted sheep following hexamethonium administration, 33% of phases III MMC originated from the duodenal bulb, 33% from the duodenum and 33% from the jejunum; in non-fasted sheep these values were equaled 50% each in the duodenal bulb and jejunum.

When atropine was injected into fasted sheep, 20% of phases III MMC originated from the duodenal bulb and 80% from the duodenum while in non-fasted animals 37.5, 37.5, and 25% of phases III started from the duodenal bulb, duodenum and jejunum, respectively. Following pirenzepine injection, 20% of recorded phases III MMC were induced from the duodenal bulb and 80% from the duodenum; in non-fasted animals 40% started from the duodenal bulb, 40% from the duodenum and 20% from the jejunum. The time lag from anticholinergic drug administration until the start of phase III MMC was dose-dependent and was the longest following hexamethonium administration. Thus, the ectopic pacemaker appears to be the most important in generation of phase III MMC and cholinergic control of phase III origin from the gastrointestinal region is important in sheep. The role of nicotinic receptors seem to be greater than that of muscarinic receptors in this area.

KEY WORDS: sheep, migrating myoelectric complex, phase III, pacemaker, feeding, cholinergic drugs, erythromycin

INTRODUCTION

The migrating motor (myoelectric) complex, MMC with its four consecutive phases, including the most characteristic phase III, have been described in detail in various animal species (Szurszewski, 1969; Code and Marlett, 1975; Ruckebusch and Bueno, 1977; Bueno and Ruckebusch, 1978b; Plaza et al., 1996a). In these animals, the substantial differences in the mode of induction and character of MMC are related to the properties of the gastrointestinal tract and feeding conditions. In monogastric animals, MMC arrives at relatively regular intervals only during the interdigestive period and is replaced by irregular activity after feeding. In ruminants, MMC is preserved during the digestive period (Ruckebusch and Bueno, 1977). Its phase III can perhaps be generated either from the stomach or from the small intestine as the so-called ectopic front (Ruckebusch and Pairet, 1984) but mostly from the duodenal bulb (Ruckebusch and Bueno, 1977). However, there are no reports of studies devoted to this problem in detail. Thus, the exact site of phase III start is not recognized in sheep. The different nature of motor activity of various segments of the gastrointestinal tract and fragmentary knowledge about the differences in controlling mechanisms between the segments imply that mechanisms initiating normal and ectopic phase III MMC can differ in sheep. Thus, the mechanisms controlling the pacemaker initiating phase III MMC in sheep are not well known.

The role of MMC in ruminants comprises both digestive and interdigestive periods, thus it is greater than in monogastric animals. Precise recognition of the mechanisms initiating phase III MMC may facilitate steering the site of phase III origin, which is important for digesta flow, and help develop methods and tools for the treatment of relevant motility disorders. It is well known that motor function of the stomach and upper small intestine is crucial for the digestive and absorptive processes in distal segments of the gut. Increasing diagnostic possibilities in veterinary medical practice represents a specific challenge for development of gastrointestinal motility studies further elucidating the complex control mechanisms, also in ruminant species. Better understanding of these processes can identify the reference point for discernment of status from physiological conditions.

Several factors participate in the induction of phase III MMC. Motilin and the cholinergic system are the most important (Pearce et al., 1978). The role of motilin seems to be less marked in ruminants than in non-ruminant species (Ruckebusch,

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1989) but this problem has not been carefully explored in sheep. Thus erythromycin, the principal drug of the group of motilides, motilin receptor agonists, was applied to assess its possible effect on the site of phase III initiation. The role of the cholinergic system can be even more pronounced in ruminants, although the role of the vagus nerve seems not to be very important (Gregory and Miller, 1984). Therefore, it might be assumed that the role of the cholinergic system in initiation of phase III MMC from the specific gastrointestinal regions in ruminants is unclear.

Feeding stimulates the cholinergic system but its precise role in the gastrointestinal pacemaker initiating phase III MMC in sheep is also uncertain. Overfeeding seems to alter the MMC pattern more profoundly than normal feeding (Bueno et al., 1977; Bueno and Ruckebusch, 1978b). More recent studies provided further data suggesting that feeding can affect gastrointestinal motility in this species (Plaza et al., 1996b). Therefore, investigations were performed in moderate fasting and non-fasting periods, with and without feeding.

Besides motilin and the cholinergic system, other mechanisms are also meaningful in the control of phase III MMC. They include opioid and serotoninergic control mechanisms and the role of other hormones like somatostatin seems to be marked in sheep (Ruckebusch, 1989).

Thus, the aim of this work was to provide new data describing the precise site of phase III start and its delay under various feeding conditions, cholinergic stimulation and cholinergic blockade, and to elucidate the role of motilin in this scope, in sheep.

MATERIAL AND METHODS

Animal preparation

The chronic experiments were performed on eight adult Polish Merino sheep weighing 40-45 kg each. 24 h fasted animals underwent surgical implantation of bipolar platinum electrodes to the distal stomach and small intestine. Seven serosal electrodes were attached onto the: 1) antrum, 4 cm proximally to the pyloric ring; 2) duodenal bulb, 6 cm distally to the pylorus; 3) duodenum, 50 cm distally to electrode 2; 4) jejunum 1, 200 cm distally to electrode 3; 5) jejunum 2, 100 cm distally to electrode 4; 6) ileum 1, 110 cm proximally to the ileo-cecal sphincter; 7) ileum 2, 100 cm distally to electrode 6 (Figure 1). The electrode wires, marked for recognition, were exteriorized 2-3 cm near the incision line on the right side of the abdomen and were fixed to the skin. Then, with the sutures completed, the animals were allowed 14 days for recovery. Drinking water was not limited. 2-4 days following the surgery, feeding with hay was started and within a few days the amount of hay reached a rate of 2 kg per animal daily. The animals were also fed with standard grain mixture (3-5 g/kg of body weight).



Figure 1. Localization of electrodes in ovine gastrointestinal tract (circle bottons) and the fragments of the recordings of continuous spiking activity (pyloric antrum) or the recordings of phase III MMC (small bowel regions) from every electrode depicted. Examples of myoelectrical recordings were taken from the same control experiment performed in non-fed and non-fasted sheep.

Explanation of symbols. Electrodes: E1 - electrode in pyloric antrum, E2 - duodenal bulb, E3 - duodenum, E4 and E5 - jejunum, E6 and E7 - ileum. Calibration 100 μ V: a - pyloric antrum (17 mm per 100 μ V, at speed of paper 2.5 mm/s), db - duodenal bulb (13 mm per 100 μ V), rsi - remaining small intestine (10.5 mm per 100 μ V). Time bar - 10 s. Further description as in the chapter Material and Methods

Experiments

During the experiments lasting 2-7 h each, myoelectric activity was recorded in habituated animals, using a multichannel electroencephalograph (Reega Duplex TR XVI, Alvar Electronic, Paris) with a paper speed of 2.5 mm/s and time constant 0.01 s to obtain clear recordings (Figure 1). The migrating myoelectric complex (MMC) and its phases were identified according to the criteria proposed by Code and Marlett (1975). At least 1-2 day intervals were allowed between two consecutive experiments

performed on the same animal. Experiments were carried out in random order and were divided into two main groups, i.e. on animals fasted 48 h and on non-fasted animals. During the control recordings in all the studied animals, at least two normal phases III MMC were recorded in most experiments. All the experiments were performed with or without feeding, before and after slow intravenous injection of agonists and antagonists of the cholinergic system. Only the first MMC cycle including the first phase III MMC that occurred following the given procedure was analyzed. Evaluation of the drug effect was started from the end of drug administration. Most experiments were repeated 2-6 times on each animal studied.

Drugs

The following drugs were used: 1) cholinergic agonists - acetylcholine chloride (ACh, Sigma) 10, 30 or 50 μ g/kg of body weight; dimethylpiperazine iodide (DMPP, RBI) 12.5, 30 or 100 μ g/kg of body weight; bethanechol chloride (Be, Sigma) 12.5, 30 or 100 μ g/kg of body weight; 2) cholinergic antagonists - hexamethonium bromide (Hx, Sigma) 1.0, 2.0 or 5.0 mg/kg of body weight; atropine sulphate (At, Polfa) 0.02, 0.1 or 0.5 mg/kg of body weight; pirenzepine dihydrochloride (Pi, Sigma) 0.02, 0.1 or 0.5 mg/kg of body weight; 3) motilin receptor agonist - erythromycin lactobionate (Er, Polfa) 12.5, 30 or 100 μ g/kg of body weight. The drugs were administered during phase II MMC, 20-30 min after termination of phase I MMC. The duration of drug infusions was: 0.5-1.0 min for low doses, 1.5-2.0 min for moderate doses and 3.0-6.0 min for high doses.

Analysis of results

MMC and its phases were identified and the duration of MMC cycles and the site of initiation of phase III MMC were analyzed in the each experimental group. The results were statistically elaborated and presented as mean values with standard deviation or as the percentage of total value in the consecutive experimental groups. Student's t-test for unpaired values was used where appropriate. Values obtained during the experiments were compared with control values obtained from the same sheep.

RESULTS

A total of 263 MMC cycles was recorded during the experiments. In fasted animals, 104 MMCs lasting 103 ± 24 min and in non-fasted animals, 159 MMCs lasting 91 ± 26 min (N.S.) were recorded during control experiments. In fasted animals, phase III MMC arrived 105.6 ± 27.0 min after feeding while in non-fasted animals phase III MMC arrived 63.7 ± 13.4 min after feeding (P<0.05).

MIGRATING MYOELECTRIC COMPLEX IN SHEEP

In fasted animals, phase III MMC originated mostly from the duodenal bulb (Table 1). Feeding tended to lower this site to the duodeno-jejunum. In non-fasted animals, phase III MMC started mostly from the duodenal bulb and the duodenum, and feeding did not markedly alter this site. In non-fed animals, about 10% of MMC phases IIIs originated from the antrum and no phase III MMC was observed in the antrum after feeding (Table 1).

TABLE 1

Site of phase III MMC origin in fasted (F) and non-fasted (N - F) sheep, before and after feeding expressed in per cent of total number of observations (n)

	Befor	e feeding	After feeding*		
	F	N - F	F	N - F	
Antrum	8.7	10.3	0	0	
Duodenal bulb	50.5	31.3	32.3	41.2	
Duodenum	29.7	39.4	38.7	35.3	
Jejunum	8.7	15.5	12.9	23.5	
Ileum	2.3	3.5	16.1	00.0010183	
n unodiscuszed -	63	102	31	1700.25	

*first phase III MMC arriving after feeding was considered



Figure 2. Scheme of myoelectrical activity of the ovine pyloric antrum (A, open irregular bars indicate continuous or almost continuous spiking activity with changeable amplitude; no distinct phase III MMC can be distinguished in this region), duodenum (D), jejunum (J) and ileum (I). Closed squares of rectangles indicate phase III MMC in these small intestinal regions. Drug (DMPP and hexamethonium bromide, Hx) administration following the control recording indicated by arrows. Four panels present four experiments performed on the same non-fed and non-fasted sheep. From top to bottom: panel 1 - DMPP administration at the dose 12.5 µg/kg i.v.; panel 2 - DMPP, 100 µg/kg; panel 3 - Hx, 1.0 mg/kg; panel 4 - Hx, 5.0 mg/kg BW.

Explanation of symbols: A - antral electrode (E1), D - duodenal electrode (E3), J - jejunal electrode (E5), I - ileal electrode (E6). Calibration 250 µV. Time bar - 30 min.

Further description as in the chapter Material and Methods

			ACh		DMPP		Be		Er	
			F	N-F	F	N-F	F	N-F	F	N-F
Lower	Α		10.8	8.6	10.4	14.2	8.4	16.6	6.4	8.4
dose ^a	DB		48.8	42.6	48.4	42.8	52.8	50.1	24.8	40.4
	D		36.2	34.8	36.6	22.4	34.0	16.6	54.6	38.4
	J		4.4	8.2	4.4	12.8	4.6	12.4	12.2	8.2
	I		0	5.6	0	6.0	0	4.2	2.0	4.2
		n	8	8	8	8	8	8	8	8
Moderate	Λ		6.8	6.4	6.6	6.2	4.2	4.2	8.4	10.4
dose ^b	DB		48.4	42.6	54.4	56.2	52.6	52.8	16.8	20.6
	D		32.8	38.4	32.2	34.4	38.2	40.2	62.6	50.6
	J		8.2	10.4	4.6	2.8	2.4	2.6	10.4	12.8
	I		3.6	2.2	2.2	0	2.2	0	2.2	6.0
		n	8	8	8	8	8	8	8	8
High	А		2.8	2.6	4.2	4.8	2.6	2.2	2.0	2.6
dose	DB		60.0	52.4	46.4	48.8	48.8	52.8	40.2	38.2
	D		32.4	34.4	42.6	40.4	38.4	40.0	46.4	48.4
	J		2.8	8.0	4.2	4.0	6.2	4.0	8.2	8.6
	I		2.0	2.4	2.2	2.0	3.6	0	2.2	2.2
		n	8	8	8	8	8	8	8	8

Site of origin of first phase III MMC arrived after various doses of cholinergic agonists and erythromycin in fasted (F) and non-fasted (N-F) sheep expressed in per cent of total number of observations (n)

A - antrum, DB - duodenal bulb, D - duodenum, J - jejunum, l - ileum. ACh - acetylcholine chloride, Be - bethanechol chloride, Er - erythromycin lactobionate

"lower doses: 10 μg/kg for ACh, 12.5 μg/kg for other drugs; ^hmoderate doses: 30 μg/kg; ^c high doses: 50 μg/kg for ACh, 100 μg/kg for other drugs. Other explanations, see chapter Material and Methods

After low doses of cholinergic stimulatory substances and erythromycin, the number of phases III MMC starting from various levels of the gastrointestinal tract was not markedly different from controls both in fasted and non-fasted sheep (Table 2, Figure 2). High doses of these drugs lowered the number of phases III MMC starting from the antrum.

Following administration of drugs blocking cholinergic receptors, only ectopic phases III MMC were observed. After administration of hexamethonium at the lower dose, all MMC phase IIIs originated from the duodenum (Figure 2). The higher dose lowered the site of start of two-thirds of these phases in fasted animals and half of phases III MMC in non-fasted animals (Table 3).

TABLE 3

Hx			Hx	At			p (0) 2000		
				F	N-F	F	N-F	F	N-F
Lower	А		82	0	0	0	0	0	0
dose ^a	DB			0	0	75.0	0.8 0 8.01	50.0	37.5
	D			100	100	25.0	75.0	50.0	62.5
	J			0	0	0	25.0	0	0
	Ι			0	0	0	0	0	0
5.9		n		8	8	8	8	8	8
Moderate	А			0	0	0	0	0	0
dose ^b	DB			33.0	50.0	20.0	37.5	20.0	40.0
	D			33.0	0	80.0	37.5	80.0	40.0
	J			0	50.0	0	25.0	0	20.0
	I			33.0	0	0	0 0	0	0
		n		9	8	10	6.6 8 8.0	10	8
High	А			0	0	0	0	0	0
dose ^c	DB			60.0	56.0	62.5	37.5	37.5	25.0
	D			40.0	44.0	0	62.5	62.5	62.5
	J			0	0	0	0	0	12.5
	Ι			0	0	37.5	0 8 0	0	0
		n		8	8	8	8 8	8	8

Site of origin of first phase III MMC arrived after various doses of cholinergic antagonists in fasted (F) and non-fasted (N-F) sheep expressed in per cent of total number of observations (n)

A - antrum, DB - duodenal bulb, D - duodenum, J - jejunum, I - ileum. Hx – hexamethonium bromide, At - atropine sulphate, Pi - pirenzepine dihydrochloride

a lower doses: 1.0, 0.02, and 0.02 mg/kg; bmoderate doses: 2.0, 0.1 and 0.1 mg/kg; chigh doses:

5.0, 0.5 and 0.5 mg/kg for Hx, At and Pi, respectively

Following atropine administration, the percentage of phases III MMC starting from the lower intestinal segments tended to increase along with the increase of the drug's dose (Table 3). A similar tendency was observed after pirenzepine administration but the results were less consistent (Table 3). Following administration of antimuscarinic drugs in fasted animals a higher percentage of phases III MMC originated from the duodenum than in non-fasted sheep.

After administration of cholinergic stimulatory substances and erythromycin, phase III MMC exhibited a tendency to arrive within a shorter time than during the relevant control periods; the results were usually dose-dependent (Table 4, Figure 2).

Administration of drugs blocking cholinergic receptors delayed dose-dependently the arrival of phase III MMC; the results obtained in non-fasted animals were more

pronounced than in fasted animals (Table 4). Low doses of pirenzepine exerted a weaker effect than higher doses. Pirenzepine administration at both higher doses provided similar results. There were no marked differences between the values obtained from the experiments performed on fasted and non-fasted sheep (Table 4). The different effect of stimulatory and inhibitory drugs on phase III start is illustrated in Figure 2.

ACh DMPP Be Er Нx Pi Λt F mean Lower ±SD dose NF mean 134* 74* ±SD n F mean Moderate ±SD NF 101* 102* dose mean ±SD n F mean High ±SD NF 256** 105* 103* dose mean ±SD n

Time lag elapsed from the end of drug administration till arrival of first phase III MMC in fasted (F) and non-fasted (NF) sheep expressed in minutes

*P<0.05; **P<0.01 vs relevant F value

other explanations, see Tables 2 and 3, and chapter Material and Methods

DISCUSSION

The obtained results suggest that the duodenum and the duodenal bulb in particular, is the most common but not the only site of initiation of phase III MMC in sheep. Ruckebusch and collaborators (Ruckebusch and Bueno, 1977; Ruckebusch and Bardon, 1984) stated that phase III MMC starts exclusively from the duodenal bulb, which remains, in part, in contrast with the present study. Spontaneous phase III MMC starting from a level below duodenal bulb has not

TABLE 4

been described in sheep. With the exception of one report (Ruckebusch and Pairet, 1984), where spontaneous phase III MMC starting just before the pyloric ring was shown, starting of phase III MMC from the stomach has not been demonstrated. The present study showed that spontaneous phase III MMC can start either from ovine pyloric antrum or from the lower parts of the small intestine decreasing the difference between ruminant and non-ruminant species in this area. In monogastrics, during the interdigestive state the acidic content can stimulate motilin release. which is responsible for occurrence of phase III MMC in the stomach (Itoh et al., 1980). It is also known that the ectopic front is guite frequent event in these species (Sarna, 1985). In ruminants, the role of motilin in the initiation of phase III MMC from the stomach seems to be limited (Ruckebusch, 1989; Plaza et al., 1996a) since the almost continuously flowing abomasal content is less acidic. However, the pH is low in the abomasum and proximal duodenum in sheep and gastric acid can inhibit abomasal motility and, in turn, initiate phase III MMC from the duodenal bulb (Gregory and Miller, 1984). These findings remain in concert with the results of Calignosan et al. (1984) who performed an immunocytochemical study and found that motilin-producing cells are absent in the ovine abomasum. The lack of a significant effect of erythromycin administration, the principal representative of motilides, upon the site of phase III origin in the present study further confirms the previous findings regarding the role of motilin in the control of MMC in sheep. However, it is unclear whether secreted acid can affect intestinal motility only via motilin release or perhaps other mechanisms also participate in this response. It is possible that motilin can be released locally by mechanical factors.

The effect of feeding on MMC in sheep was reported by several authors (Bueno and Ruckebusch, 1978b; Lester and Bolton, 1994). Principally, feeding does not abolish MMC in ruminants but, as in monogastric animals it appears to stimulate the cholinergic system and digestive hormone release (see below), thus involving several regulatory mechanisms. Therefore, the precise interpretation of the effect evoked by feeding is difficult. Food is a strong stimulus to gastrointestinal motility, thus the lack of phase III MMC in the antrum observed in the present study during control experiments after feeding coincides with the decreasing number of phases III MMC in the antrum along with the increased doses of stimulatory substances. Stronger stimulation can also trigger factors inhibiting phase III MMC in the antrum and/or factors stimulating phase III MMC in the small intestine. As was reported by Ruckebusch and Pairet (1984), antral and duodenal motility are coordinated. When phase III MMC is present in the duodenum, antral activity is periodically ceased. Food-provoked abomasal distension might induce abomasal emptying thus stimulating the propulsive motility but the effect of gastric distension on initiation of phase III MMC has not been reported. The role of cholinergic mechanisms (Bueno and Ruckebusch, 1978a; Ruckebusch et al., 1987) and direct or indirect release of gastrointestinal hormones including gastrin, cholecystokinin, pancreatic polypeptide, somatostatin and insulin (Walsh, 1994; Plaza et al., 1996a,b) can be considered important events in these circumstances.

Acetyleholine and DMPP administration did not exert any significant effect on the site of phase III MMC initiation. Nicotine can inhibit antral motility probably due to its action on nicotinic receptors present in adrenergic ganglia. Thus, this action can neutralize the influences upon the cholinergic intramural ganglia of the enteric nervous system. Low and moderate doses of hexamethonium inhibited phase III MMC in the gastroduodenal region more strongly than the muscarinic antagonists. Hexamethonium inhibited the arrival of phase III MMC for a longer period than the antimuscarinic drugs. The nicotinic receptors are present in intramural ganglia projecting to the smooth muscles with the efferent neural fibres that are cholinergic in part. Muscarinic receptors are mostly localized closely to the smooth muscle. Thus, the effects mediated by intramural ganglionic nicotinic receptors could be transmitted through the efferent neural fibres to a broader region than muscarinic effects and be more pronounced. The present study provided meaningful evidence that the cholinergic system is directly responsible for the initiation of phase III MMC and that the role of nicotinic receptors is more pronounced than that of muscarinic receptors in this area.

There were no marked differences between the effects of atropine and pirenzepine on the site of the origin of phase III. Atropine is an unspecific muscarinic blocker while pirenzepine can distinguish between some muscarinic receptor subtypes. Pirenzepine was thought to be able to engage principally the M, cholinergic receptor subtype. It was found by Schiavone et al. (1989) that pirenzepine at a small dose blocked M, cholinergic receptors influencing MMC in the dog. More recent data indicate that pirenzepine can act also on other muscarinic receptor subtypes and it was confirmed that atropine is an unspecific muscarinic receptor antagonist (Shi and Sarna, 1997). The obtained results suggest that were no specific differences in pirenzepine action when the drug was given in various doses. Thus, pirenzepine exerted its action through the muscarinic receptors other than of M, subtype. Almost nothing is known regarding the possible role of muscarinic receptor subtypes in the inhibition of phase III MMC and the site of the origin of phase III MMC in sheep. A recent study provided some data that cholinergic muscarinic receptor subtypes can differ in their role in gastroduodenal coordination in this species (Romański and Sławuta, 2001). Therefore, the problem warrants further investigation.

It is well known that not only motilin and cholinergic mechanisms are important for the site of phase III origin, i.e. for the initiation of phase III (Sarna, 1985; Ruckebusch, 1989). Opioid and serotoninergic mechanisms and some gut hormones, including somatostatin were also reported to be important (Ruckebusch and Bardon, 1984; Plaza, 1996a). As motilin action can be exerted directly on the smooth muscles and indirectly, through the cholinergic system, there is also evidence for the cooperation between other important mechanisms in their control of gastrointestinal motility due to the presence of cholinergic interneurons within the enteric nervous system connected with non-adrenergic non-cholinergic (NANC) neurons (Vizi et al., 1984; Grider, 1994). The effect of such cooperation can either be stimulatory or inhibitory, which can be illustrated by the reported inconsistent effect of vagotomy on gastrointestinal motility (Gregory et al., 1984; Malbert and Ruckebusch, 1989). Thus, it can be concluded that the cholinergic system may participate directly and indirectly in the control of gastrointestinal motility, including the MMC pattern and further extensive studies are necessary to elucidate its precise role in sheep.

The presented results indicate that the duodenal pacemaker area is the most important in the initiation of phase III MMC in sheep and the role of cholinergic mechanisms in the control of this event is complex. It might be more pronounced in the antrum than in the small intestine where other mechanisms may have the principal role in the initiation of phase III MMC (Ruckebusch, 1989).

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STRESZCZENIE

Cholinergiczna kontrola rozrusznika inicjującego fazę III wędrującego kompleksu mioelektrycznego u owcy

W celu ustalenia rejonu inicjowania fazy III wędrującego kompleksu mioelektrycznego (MMC) i sprecyzowania roli cholinergicznych receptorów nikotynynowych i muskarynowych w inicjowaniu wspomnianej fazy, przeprowadzono chroniczne doświadczenia na 8 owcach z wszczepionymi elektrodami bipolarnymi do ściany jamy odźwiernikowej i jelita cienkiego. Aktywność mioelektryczną z tych rejonów rejestrowano przy pomocy wielokanałowego elektroencefalografu, przed i po powolnym dożylnym podaniu cholinergicznych agonistów i antagonistów oraz agonisty receptora motylinowego, laktobionianu erytromycyny. Fazy MMC różnicowano stosując kryteria zaproponowane przez Code'a i Marlett. Łącznie obserwowano 263 cykle MMC, trwające odpowiednio u owiec głodzonych i nie

głodzonych 103±24 min i 91±26 min. U owiec głodzonych start fazy III MMC następował w 8,7% z jamy odźwiernikowej, 50,5% z opuszki dwunastnicy, 29,7% z dwunastnicy, 8,7% z jelita czczego i 2.3% z jelita biodrowego. U owiec nie głodzonych odsetek rozpoczynających się faz III wynosił odpowiednio: 10,3; 31,3; 39,4; 15,5 i 3,5. Po podaniu środków antycholinergicznych faza III MMC w rejonie jamy odźwiernikowej nie występowała. Po podaniu heksametonium start fazy III następował u owiec głodzonych w 33% z opuszki dwunastnicy, w 33% z dwunastnicy i w 33% z jelita biodrowego, a u nie głodzonych w 50% z opuszki dwunastnicy i w 50% z jelita czczego. Po podaniu atropiny start fazy III następował u owiec głodzonych w 20% z opuszki dwunastnicy i w 80% z dwunastnicy dalszej, a u owiec nie głodzonych w 37,5% z opuszki dwunastnicy, w 37,5% z dwunastnicy i w 25% z jelita czczego. Po zastosowaniu pirenzepiny faza III rozpoczynała się u owiec głodzonych w 20% z opuszki dwunastnicy i w 80% z dwunastnicy, a u nie głodzonych w 40% z opuszki dwunastnicy, w 40% z dwunastnicy i w 20% z jelita czczego. Długość okresu od podania środka antycholinergicznego do pojawienia się fazy III MMC zależała od dawki i była najdłuższa po podaniu heksametonium. Pozaszczytowy rozrusznik wydaje się być zatem najbardziej istotny w inicjowaniu fazy III MMC u owey, podczas gdy układ cholinergiczny wydaję się mieć najwiekszy wpływ na iniciowanie fazy III MMC z rejonu jamy odźwiernikowej u tego gatunku. Rola nikotynowych receptorów wydaje się być większa w tym zakresie niż receptorów muskarynowych.