Phasic organization of the migrating motility complex

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ABSTRACT

The article presents some old and new data regarding organization of the migrating motility complex (MMC) and its phases. The MMC cycle is one of two main motility patterns present in the gastrointestinal tract of humans and animals. The MMC is composed of three or four phases numbered consecutively. Both generation and organization of the cycle are still incompletely understood. Any progress in this area can help in further recognition of mechanisms of pattern generation and arrival what is of clinical importance since many MMC disturbances are observed. Thus the article presents some old and new data further explaining the role of phase 3 of the cycle and suggesting revised MMC organization. Its inactive phase is commonly labeled as phase 1 of the MMC, implying that the entire MMC pattern is initiated just during this phase. Irregular phase 2 could represent the spontaneous activity. The highly propulsive and specific phase 3 of the MMC commences in the course of phase 2b and apparently is embedded in this phase. Phase 3 is thus often considered the most characteristics and important in the cycle and it can be assumed that the triggering of phase 3 of the MMC initiates the appearance of the whole MMC cycle, at least when a given locus is considered. Phase 4 of the MMC, also irregular and thus similar to the phase 2, may represent the terminal part of phase 2. Therefore the numbering of the classical phases 1, 2a, 2b, 3 and 4 as phases 2, 3a, 3b, 1, and 3c, respectively seems more relevant. It is believed that presented view of the MMC organization will help in a better understanding of the character of the cycle.

Keywords: migrating motility complex, organization, controlling mechanism, dog, sheep

RÉSUMÉ

Organisation phasique du complexe moteur migrant

L'article présente quelques données anciennes et nouvelles concernant l'organisation du complexe moteur migrant (CMM) et ses phases. Le cycle du CMM est l'un des deux principaux motifs de motilité présents dans le tractus gastro-intestinal des humains et des animaux. Le CMM se compose de trois ou quatre phases numérotées consécutivement. La génération et l'organisation du cycle sont encore incomplètement compris. Cet article présente quelques données anciennes et nouvelles expliquant le rôle de la phase 3 du cycle et suggérant une organisation révisée des CMM. La phase inactive est communément nommée phase 1 du CMM. La phase irrégulière 2 pourrait représenter une activité spontanée. La phase 3 hautement propulsive et spécifique peut commencer au cours de la phase 2 et est apparentemment incorporée à cette phase. La phase 3 est donc souvent considérée comme la plus importante dans le cycle et on peut supposer que le déclenchement de la phase 3 déclenche l'apparition de tout le cycle. La phase, également irrégulière et donc semblable à la phase 2, peut représenter la partie terminale de la phase 2. Par conséquent, la numérotation des phases classiques 1, 2, 3 et 4 en tant que phases 2, 3a, 3b, 1, et 3c, respectivement, semblent plus pertinente pour aider à une meilleure compréhension du CMM.

Mots-clés : physiologie, complexe moteur migrant, chien, mouton

Introduction

The whole digestive tract, from mouth to anus, exhibits motor activity due to the presence of intramural 1-3 smooth muscle layers located between submucosa and serosa. Both the anatomical features and motor functions of the stomach and small intestine are related to their physiological roles and exhibit great variability [24, 80]. The gastrointestinal motility is principally composed of two types of events. First comprises the myoelectricity and the second represents the mechanical activity. The former arrives as the slow (slow waves) and fast (spikes forming the spike bursts) changes in transmembrane potentials [64]. The presence of the slow waves may facilitate induction of the spike bursts that are directly responsible for phasic contractions mostly of the circular muscle layer, but longitudinal muscle contractions are also meaningful [53]. Phasic contractions are less effective in digesta mixing and propulsion than longer duration (giant) contractions unless are organized in longer series. The longest (tonic) contractions exhibit no myoelectric correlates and are not linked with the slow waves [54]. Therefore, the myoelectrical and motor recording methods can be applied in vitro or in vivo study of the gastrointestinal motility [37, 52]. These methods utilizing the implanted serosal or mucosal electrodes and strain gauge force transducers are invasive, especially when are mounted on surgically prepared gastrointestinal segments or when other surgical techniques are used [22, 27, 29, 76, 81]. Manometry and radiotelemetry are less invasive. All these methods can also be applied for the assessment of the sphincteric function [13, 70]. From the clinical point of view, the minimally invasive (x-ray methods, scintigraphy) or non-invasive (ultrasonography, magnetic resonance imaging) methods are the most useful. For diagnosis of the gastrointestinal motility disorders in man and animals [1, 79], more general information regarding the digesta movement is more important than the recording of individual contractions, slow waves and spike bursts. Therefore, several imaging methods for the study of gastric emptying and intestinal transit as well as electrogastrography predominated in clinical motility studies, particularly in man, dog and cat [38, 75, 78, 81, 86]. When the arrangement of phasic contractions or their myoelectric correlates is considered, the gastrointestinal motility can be strictly organized in...
the specific motility patterns. Nevertheless, it can vary considerably regarding the animal species, gastrointestinal segments and feeding conditions. In fed non-ruminant animals, the arrangement of the spike bursts or contractions is irregular since not every slow wave is superimposed with the spike burst. The spike bursts and contractions can occur separately or in the short series (the fed pattern [54, 80]). In fasted non-ruminant species the gastrointestinal motility is organized in cycles called the migrating motility complexes (MMCs) [63]). Thus feeding can disrupt the MMC in man and dog while in rat and pig the disruptive effect is related to feeding frequency [44, 51]. No MMC is present in the cat. The greatest role in these achievements regarding human and canine motility can be ascribed to the investigators from the USA (Mayo Clinic and University of Wisconsin [8, 29, 30, 63, 76]). The character of motility in ruminants may differ in part from that in monogastrics and the question arises whether the differences of the antral and small-intestinal motility between ruminants and non-ruminants are greater than the differences among various non-ruminant species. Sheep is the most common ruminant animal used for the gastrointestinal motility study including forestomachs [61]. Since the interdigestive period does not occur in this species, the MMC arrives in ovine small bowel almost independently of feeding conditions. Overfeeding also exerts minor effect upon the ovine MMC [6]. In the Western Europe, the French group from Toulouse has the greatest contribution to the recognition of the gastrointestinal motility and MMC in ruminants and other species including dog [5, 6, 50]. For example, to my knowledge, these investigators published more papers on gastrointestinal motility in sheep than all other authors. They characterized the motor function of the whole gastrointestinal tract and the controlling mechanisms in sheep [3, 5, 6, 47-49]. These authors used sheep, dog and other adult or young animal species for physiological, pharmacological and nutritional investigations [2, 4, 6, 16, 17].

The interdigestive motility pattern (MMC) regularly occurs in man and several animal species. Its organization is cyclic [8, 63]. The MMC cycle is composed of three or four phases, always sequenced in the same order. During the inactive phase 1 of the MMC, only single and sparse contractions can occur. In the course of phase 2 the frequencies, durations, and amplitudes of irregularly arriving contractions gradually increase. Since phase 2 is often longer than the other MMC phases, it was suggested to divide it into phase 2a and 2b [11]. During phase 3 of the cycle the maximal intensity of contractions occurs and they are arranged in the most regular fashion. Phase 4 of the MMC is not always observed and represents irregular transient motility arriving between phase 3 and phase 1 of the next cycle [8]. The MMC arrives in monogastrics only in the fasting state, but in ruminants it also occurs during the digestive state, which makes its role in gastrointestinal transport even more important [48]. The pattern is thus quite well defined and characterized, although many questions including its organization were recognized only ostensibly.

The studies on the organization of interdigestive motility are continued [7, 28]. However, the question has not yet been sufficiently explored. The knowledge regarding the MMC control mechanisms is still also fragmentary. Much more is known about the mechanisms initiating phase 3 of the MMC than about the mechanisms responsible for its maintenance and cessation. A deeper understanding of the organization and control mechanisms of the MMC seems desirable since the pathogeneses of several abnormalities of this pattern occurring in various species are largely unknown [20, 21]. Thus it is still difficult to establish what is the exact role of the MMC phases (especially that of phase 3) in the generation of the cycle. There is some reported data suggesting that the generation of phase 3 of the MMC is more important that may be expected and thus the MMC phase numbering can be different. The modified division of the MMC into invariably three phases (along with one of these phases further subdivided or not) might facilitate understanding the real organization of the MMC cycles. The presentation of these scientific arguments regarding MMC phase numbering represents the first aim of this review. Accordingly, the new concept regarding the MMC organization is presented and this new proposal may prompt and direct further study upon the pattern generation and organization. It is still too early to draw the definite conclusions as to the organization of the MMC. Also its generation mechanisms are still unknown. This article presents some aspects of MMC organization, generation, and controlling mechanisms, but also suggests that the phase 3 initiates the complex. The presented concept regarding the modified sequencing of the MMC phases seems to be more argued than the current views on MMC organization and classical phase numbering. However, the presented MMC organization is still hypothetical although remains in accordance with the current knowledge.

Organization of the MMC pattern - Phase 1 versus phase 3

The detailed organization of the MMC cycle is incompletely understood [19, 28]. Classical observations concerning the arrangement of the MMC phases were based on the visual inspection of myoelectrical recordings. The proposed numbering of the MMC phases was related in part to the incidence of spiking activity. From simple arithmetical point of view consecutive phase numbering (Roman or Arabian) appeared to be logical and easy to remember, but this sequence is not supported by scientific arguments. Nonetheless, the proposed sequencing of the MMC phases and the three- or four-phase organization of the MMC has been widely accepted. Van Schelven et al [77] stated that the convenient sequential classification of the MMC into phase 1, phase 2, and phase 3 is partly arbitrary. It might thus be more correct to classify the MMC phases into a ‘quiescent phase,’ ‘irregular phase,’ and ‘activity front’ than to number them from 1 to 4. The other terms of the MMC phases, also applied by various authors, exist in the literature, but classical phase numbering was always the same and mostly Roman
numbering is applied [65, 74, 80]. This terminology suggests that phase 1 of the MMC begins the whole cycle and that phase 4 is a separate part of the MMC. However, Lang et al [30] and Sarna and Otterson [57] proposed that phase 1 might be controlled by the preceding phase 3 of the MMC. A similar conclusion was drawn by Luiking et al [33]. If the actual concept explaining the occurrence of phase 1 of the MMC, as the refractory period [55] or the resting period [82] is correct, it may mean that not the phase 1, but the arrival of phase 3 initiates the whole cycle. Therefore, as phase 1 may not be actively induced, there is no reason to assume that it begins the whole cycle. When phase 3 is absent, no clear phase 1 can be observed and phase 4 is indistinguishable. It was suggested that migrating membrane complex oscillators might generate only the phase 3 [30]. Therefore, phase 1 of the MMC could be evoked by the ascending inhibitory influences caused by distally migrating phase 3 activity. If so, it is unlikely that phase 1 can begin the whole cycle. Thomas et al [68] proposed the general view that the length of the MMC cycle is governed by the rate of recovery of synaptic efficacy, while some data presented there suggest a distinct role of phase 3 of the MMC in the generation of the cycle. The duration of phase 3 is more stable unlike other MMC phases what further confirms this view. Initially, Szurszewski [63] suggested that the MMC is represented only by phase 3, but it is generally accepted that phase 3 is one of three or four MMC phases. As it was mentioned above, phase 3 is apparently the most characteristic and important phase of the cycle and it is responsible for the efficient remnant digesta transport [54]. When MMCs arrive during the postfeeding period, they usually begin with phase 3 [31, 39, 50, 60]. As these observations suggest that the subsequent MMC cycle may also start with phase 3, its role in MMC organization seems to be the most important.

Taken together, it appears that phase 3 is more typical and important for the MMC than phase 1 and it is less probable that phase 1 initiates the whole MMC cycle.

**Phase 3 Induction and cessation - Roles of control mechanisms**

The mechanisms inducing the MMC cycles are still uncertain although they appear to be very composed [9, 66]. It has not been convincingly demonstrated whether the occurrence of MMC phases during the interdigestive period is the direct result of mucosal stimulation by the luminal content (or lack of this stimulation) involving the neural endings and/or is evoked by the neural or neuroendocrine stimuli accompanied by changes in gastrointestinal hormone levels. The role of a ‘biological clock’ in the arrival of the MMC has also been postulated [51, 83]. In this situation, the role of the mucosal contact with luminal content must be of secondary importance. However, it has been demonstrated that phase 3 is triggered by nerve firing, but it is not established which neural centers initiate this firing in normal conditions [54]. The report of Miolan and Roman [34] suggests that firing was transmitted via the vagus nerve.

In turn, the cholinergic blocking drugs such as atropine, pirenzepine, and hexamethionium were able to evoke a premature phase 3, but they may simultaneously inhibit the other contractions [58, 73]. Thus, phase 3 appears distinct from the other active phases of the MMC. The recent reports also suggest that the mechanisms inducing phase 3 could differ in the stomach from those in the small bowel [10, 35]. Therefore, the mechanism of the initiation of phase 3 appears to be different, at least in part, from the even less known mechanism evoking phase 2 of the MMC and it is possible that these two phases can be evoked independently. In addition, phase 3 arrives in the course of or just after the phase 2. Lang et al [30] suggested that in the small bowel phase 2 of the MMC represents the spontaneous motor activity. The same view could concern phase 4 of the MMC as well. Summarizing this part it can be stated that factors inducing phase 2 and phase 3 of the MMC can be partly different and still are poorly recognized.

The regularity and character of phase 3 of the MMC are rather stable, at least at a given locus, unlike those in the other MMC phases and apparently also of the whole cycle [14]. The appropriate mechanisms, responsible for the duration (i.e. the maintenance) of phase 3 and probably responsible for the cessation of this phase, thus appear to exist and to be quite precise. The partly recognized role of the cholinergic system in the control of phase 3 and also of phase 2 of the MMC can support these suggestions. It was demonstrated that anticholinergic drugs inhibit gastrointestinal motility rather effectively [5, 42, 57, 58, 73]. Cholinergic excitatory neurons predominate in the small bowel, while humoral mechanisms seem to play a more evident role in the stomach [26, 33]. When small or moderate doses of anticholinergic drugs are administered systemically or locally in the course of phase 2 of the MMC, they primarily inhibit motor or myoelectric activity and may then induce the opposite response [40, 41]. When the same dose of atropine or pirenzepine, that was capable of inhibiting ovine small bowel motility during phase 2, was given in the course of phase 3 of the MMC, no inhibitory effect was observed [41]. Fig. 1 illustrates the lack of inhibitory effect of atropine given at a low or moderate dose in the course of phase 3 of the MMC in the ovine jejunum. Atropine did not alter the duration of phase 3 as well. The effective drug doses interrupting phase 3 of the cycle must thus be greater than the doses interrupting phase 2 and delaying phase 3 when applied before its arrival [41, 42]. It has also been undoubtedly demonstrated that the contractions forming phase 3 are maximal and are the greater than during phase 2 of the MMC [68]. Furthermore, the phase 3 is more uniform and regular than phase 3 of the MMC. These data further argue that at least some of the neural mechanisms controlling phase 2 might be different from the mechanisms controlling phase 3 of the MMC.
The analysis of phase 3 recordings also suggests that in the course of phase 3 of the MMC the putative control mechanisms prevent phase cessation for some time and the suppression of contractions below certain level [41, 42]. Thus it can be interpreted as a specific ‘positive refraction’, while the putative refraction inhibiting the occurrence of contraction may be called ‘negative refraction’. Both can be absolute or relative. Pure neural or neurohormonal mechanisms controlling phase 3 of the MMC can be involved herein. Two groups of neurohormonal mechanisms can be distinguished: neural mechanisms cooperating with hormones (involving the neuroendocrine pathways) and neural mechanisms mediated directly by neuromodulators [85].

Among the neurohormonal factors inducing the arrival of phase 3 of the MMC, both excitatory, such as motilin, serotonin, and ghrelin [15, 67] and inhibitory substances, such as cholecystokinin, pentagastrin and neurotensin [71, 84], have been found. Several other factors inducing phase 3 of the MMC were described further [44]. These substances were found to affect spontaneous contractions (related to phase 2 of the MMC), but not in all cases. It has been shown that insulin, tachykinins, and perhaps melatonin affect phase 2-related contractions rather without direct influencing of the phase 3 of MMC [32, 69, 72]. These factors do not appear to affect phase 3 of the MMC. The inhibitory effects of some peptide hormones upon the phase 3 of the MMC were more efficient than the cholinergic blockade. When cholecystokinin-octapeptide was administered, the same doses, unlike the small doses of atropine, interrupted the already existing phase 3 (K. W. Romanski, personal communication) and delayed the forthcoming phase 3 of the MMC in the human, canine, and ovine small bowel [23, 43]. The good correlation of serum motilin peaks and phase 3 of the MMC might be considered as another explanation of phase 3 initiation and maybe also, to some extend, its maintenance at least in the stomach [25, 59]. Increasing motilin release may excite the motilin receptors in smooth muscle cells and/or receptors located on appropriate intramural neurons inducing phase 3 of the MMC. When the raise in plasma motilin concentration is sufficient, phase 3 is still present. In turn, when plasma motilin falls below the threshold level, phase 3 of the MMC is inhibited at least when no other natural stimuli are active at the moment. It is believed that motilin’s role in the initiation of the gastric phase 3 is evident, at least in man [10]. Concomitant action of motilin with other regulators is very probable. In man and animals it can cooperate with ghrelin, although the contribution of other factors cannot be excluded [9, 36]. It is possible that neural firing, triggering phase 3 of the MMC, first induces motilin and also serotonin release within the enteric nervous system and to the intestinal lumen [65, 66]. Therefore it seems likely that the triggering mechanism of phase 3 is distinct from the mechanism responsible for its maintenance. The mechanism responsible for cessation of this MMC phase remains unknown. These mechanisms seem to involve mostly peptidergic component and the role of pure cholinergic influences apparently is reduced. Furthermore, various chemical regulatory factors can influence the arrival and cessation of phase 3 and of phase 2 suggesting the presence the distinct mechanisms controlling these two MMC phases. They can be linked with the induction of the fed pattern as well [57, 80].

In summary, the knowledge regarding the MMC control mechanisms is incomplete. Much more is known about the mechanisms initiating phase 3 of the MMC than about the mechanisms responsible for its maintenance and cessation. It is possible that these mechanisms can be distinct, exhibiting at least few common elements.

**MMC organization**

The specific signals evoking phase 3 become efficient in the course of late phase 2 of the MMC when refraction is no longer present in the gut [56]. While during phase 1 the absolute refraction can occur, during phase 2a the presence of relative refraction can be admitted. Therefore, during phase 2b, the efficient stimulus can be relatively weaker than that during phase 1 or even during phase 2a of the MMC, and this may help to understand why phase 3 is usually triggered rather at the end of phase 2 of the MMC. Since the newly induced phase 3 displaces phase 2 for few minutes, it can be postulated that phase 3 is embedded in phase 2 (mostly in phase 2b) of the MMC. After cessation of phase 3 of the MMC, phase 2 - especially terminal fragment of phase 2b - might return for a relatively short period (which is classically interpreted as phase 4 of the MMC) but not always. Then the new absolute refractory period (i.e. classical phase 1 of the MMC) arrives. Its forthcoming might be understood as
poststimulatory inhibition (inhibitory rebound) as well. The
duration of phase 2 of the MMC does not correlate with the
duration of phase 4 since the duration of the latter phase is
often very variable or this phase may be absent altogether.
When the duration of phase 4 of the MMC is longer (lasting
a several minutes or more), as it is sometimes observed,
for example in dogs receiving bile acid infusions, phase 4
closely resembles more active part of phase 2 [46]. Similar
observations were performed in sheep (K. W. Romański,
unpublished) and in dogs [62]. Table 1 summarizes the
effects of some principal compounds upon the MMC. If
these observation-based assumptions are correct, it can be
expected that the character of phase 4 of the MMC should
resemble phase 2b rather than phase 2a, which seems to be
the case at least in the dog and sheep (Fig. 2). When phase
3 of the MMC is triggered just at the end of phase 2, the
irregular activity, interpreted so far as separate phase 4, does
not occur. This concept is illustrated in Fig. 3. Accordingly,
only three phases of the MMC, i.e. the classical phase 3, phase
1, and phase 2, can be distinguished because the MMC cycle,
according to the presented concept, may begin from the
classical phase 3 (Fig. 4). The classical phase 1 can be called
‘phase 2’ of the MMC. The classical phase 2 (subdivided into
phase 2a and 2b or not) can be called ‘phase 3’ of the MMC
and this phase can be subdivided or not into phase 3a, 3b or
possibly also phase 3c of the MMC. The latter subphase can
replace classical phase 4 while present. The classical phase 3
may occur as ‘phase 1’ of the MMC (Fig. 4). This phase
may be called phase 1 of the MMC for at least two reasons.
Firstly, the MMC cycle appears to originate from this phase.
Secondly, the classical phase 3 of the MMC is considered as
the most important and the most characteristic phase of the
cycle. It is well known that no classical phase 3 is present, no
MMC cycle could be identified or at least it is not mentioned
that the MMC cycle is present.

**Concluding remarks**

The organization and mechanisms controlling the
interdigestive motility pattern are incompletely understood
since they are very complex, and therefore still require
extensive study. It might be expected that the views presented
here can contribute to increasing the knowledge of the
organization and control of the MMC, including its phase 3,
and provoke appropriate investigations leading directly to a
further understanding of the precise character of this type of
motor activity.

### Table 1: Principal factors affecting directly or indirectly the migrating motility complex (MMC) and its phase 3 in various animal species.

<table>
<thead>
<tr>
<th>Action</th>
<th>Type of factor</th>
<th>Influencing factor</th>
<th>Effect on MMC and its phase 3</th>
<th>Animal species</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulatory effects</td>
<td>Neural</td>
<td>At*, Hx*</td>
<td>Induction of phase 3</td>
<td>Dog</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td></td>
<td>At*, Hx*</td>
<td>Induction of rebound excitation*</td>
<td>Sheep</td>
<td>5, 41</td>
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<tr>
<td></td>
<td></td>
<td>Pi <em>, Te</em></td>
<td>Low doses: induction of premature phase 3</td>
<td>Dog</td>
<td>12, 58</td>
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<tr>
<td></td>
<td></td>
<td>Pi*</td>
<td></td>
<td>Sheep</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Hormonal, neurohormonal</td>
<td>Motilin</td>
<td>Induction of phase 3</td>
<td>Man, dog</td>
<td>51</td>
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<tr>
<td></td>
<td></td>
<td>Serotonin</td>
<td></td>
<td>Dog</td>
<td>67</td>
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<td></td>
<td></td>
<td>Ghrelin</td>
<td></td>
<td>Rat</td>
<td>15</td>
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<tr>
<td>Other</td>
<td>Fasting</td>
<td></td>
<td>Induction of MMC cycles</td>
<td>Man, dog</td>
<td>8, 63</td>
</tr>
<tr>
<td></td>
<td>Neural</td>
<td>At, Hx, Pi</td>
<td>Prolongation of MMC cycle</td>
<td>Man, dog</td>
<td>12, 51</td>
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<td></td>
<td></td>
<td>Other anticholinergics</td>
<td></td>
<td>Sheep</td>
<td>5, 42</td>
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<td></td>
<td></td>
<td></td>
<td>Dog</td>
<td>12</td>
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<td></td>
<td>Guinea pig</td>
<td>18</td>
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<td></td>
<td></td>
<td></td>
<td>Sheep</td>
<td>5</td>
</tr>
<tr>
<td>Inhibitory effects</td>
<td>Hormonal, neurohormonal</td>
<td>CCK</td>
<td>Prolongation of MMC cycle, delaying of phase 3</td>
<td>Man, dog</td>
<td>3, 84</td>
</tr>
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<td></td>
<td></td>
<td>Gastrin</td>
<td>Change of MMC to fed pattern</td>
<td>Sheep</td>
<td>43</td>
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<tr>
<td></td>
<td></td>
<td>Neurotensin</td>
<td></td>
<td>Dog</td>
<td>84</td>
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<tr>
<td>Other</td>
<td>Feeding</td>
<td></td>
<td>Disruption of MMC</td>
<td>Man, dog</td>
<td>8, 63</td>
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<td></td>
<td>Bile acids</td>
<td></td>
<td>Prolongation of MMC cycle</td>
<td>Dog</td>
<td>46</td>
</tr>
</tbody>
</table>

Explanations: ‘secondary effect,’ * rebound excitation partly resembles phase 3 of the MMC, At - atropine, Hx - hexamethonium, Pi - pirenzepine, Te - telenzepine, CCK - cholecystokinin.
Figure 2: Similarities of phase 4 of the MMC to phase 4 in the duodenum and jejunum.

Explanations: A – representative scheme of the individual spike bursts in fasted dog based on the control experiments (Romański and Peeters, 1989, unpublished); B – representative scheme of the individual spike bursts in fasted sheep (control experiments). Calibration: 200 μV, time: 30 s.

Figure 3: The new concept of the organization of the MMC phases and their generation.

Explanations: There are three possibilities of induction of phase 3 of the MMC in relation to phase 2. A – phase 3 of the MMC is "embedded" at the end of phase 2 and the irregular motor activity, currently interpreted as phase 4, follows phase 3. Therefore, phase 4 is a prolongation of phase 2 of the cycle. When first phase 3 of the MMC occurs after feeding it arrives during the fed pattern; B – phase 3 of the MMC is triggered just at the end of phase 2; thus the end of phase 3 arrives at the same time as the end of phase 2. Therefore, no phase 4 of the MMC can be observed in this case since phase 3 directly changes into phase 1; C – phase 3 of the MMC arrives with some delay and the end of phase 2 lies approximately in the middle of phase 3. Thus no phase 4 can be observed as well.

Figure 4: Organization of the MMC: examples of old and new concepts.

Explanations: Upper panel presents the MMC without phase 4; part A – classical division of the MMC cycle into three phase 1, 2 and 3. Classical phase 2 can be subdivided into phase 2a and 2b or not. Part B – proposed concept of new phase numbering relevant to part A of this panel. Lower panel presents the MMC with phase 4; part A – classical division of the MMC cycle into four phases; part B – proposed concept of new phase numbering with further subdivision of ‘phase 3’. In this case the ‘phase 3’ can be subdivided into three subphases. ph. – MMC phase. For further explanations, see the text.
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