ELECTROGASTROGRAPHY
clinical applications

ELECTROGASTROGRAFIE

klinische toepassingen

PROEFSCHRIFT

TER VERKRIJGING VAN DE GRAAD VAN DOCTOR IN DE
DE GENEESKUNDE
AAN DE ERASMUS UNIVERSITEIT ROTTERDAM
OP GEZAG VAN DE RECTOR MAGNIFICUS
PROF. DR. A.H.G. RINNOOY KAN
EN VOLGENS BESLUIT VAN HET COLLEGE VAN DEKANEN.
DE OPENBARE VERDEDIGING ZAL PLAATSVINDEN OP
VRIJDAG 16 JANUARI 1987 OM 14.00 UUR.

DOOR

HAN GELDOF

GEBOREN TE MIDDELBURG

PROMOTIECOMMISSIE:

PROMOTOR:	PROF. J.H.P. WILSON
PROMOTOR:	PROF. DR. IR. C.J. SNIJDERS
OVERIGE LEDEN:	PROF. DR. G.N.J. TIJTGAT PROF. DR. H.A. BRUINING

Aan mijn ouders,
die de basis hebben gelegd voor een loopbaan die ik tot op de dag van vandaag als zinvol en gelukkig heb ervaren.

Aan Ineke,
zonder haar steun was het onmogelijk geweest.

Contents

List of abbreviations XI
1. Introduction and objectives of the study 1
2. Physiology of the stomach 5
   2.1. Introduction 5
   2.2. Anatomical considerations 5
   2.3. Myoelectrical properties of gastric smooth muscle 6
   2.4. Normal patterns of gastric motility 9
   2.5. Control mechanisms of gastric motility 10
3. Literature survey 13
4. Electrogastrography 17
   4.1. Introduction 17
   4.2. Technique of recording 17
   4.3. Signal analysis and data presentation 20
   4.4. Standard recording procedure 27
   4.5. Accuracy and reliability of electrogastrography 28
      4.5.1. Abstract 28
      4.5.2. Introduction 28
      4.5.3. Materials and methods 30
      4.5.4. Results 35
      4.5.5. Discussion 38
      4.5.6. References 43
5. Electrogastrography in healthy subjects 45
   5.1. Introduction 45
   5.2. Electrogastrographic characteristics of the interdigestive migrating complex in man 46
      5.2.1. Abstract 46
      5.2.2. Introduction 46
      5.2.3. Materials and methods 48
      5.2.4. Results 52
      5.2.5. Discussion 57
      5.2.6. References 60
   5.3. Gastric myoelectrical behaviour in healthy subjects studied by standard electrogastrography 63

5.3.1. Introduction 63
5.3.2. Materials and methods 63
5.3.3. Results 64
5.3.4. Discussion 69
5.4. Effects of gastric bypass operation and sham feeding on the postprandial myoelectrical behaviour 72
5.4.1. Introduction 72
5.4.2. Materials and methods 73
5.4.3. Results 75
5.4.4. Discussion 79
6. Electrogastrography in patients 81
6.1. Gastric myoelectrical disturbances in the fasting and postprandial state in gastric ulcer patients: an electrogastrographic study 81
6.1.1. Abstract 81
6.1.2. Introduction 81
6.1.3. Materials and methods 83
6.1.4. Results 88
6.1.5. Discussion 97
6.1.6. References 104
6.2. An electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting 108
6.2.1. Abstract 108
6.2.2. Introduction 108
6.2.3. Materials and methods 110
6.2.4. Results 114
6.2.5. Discussion 124
6.2.6. References 127
6.3. Effects of highly selective vagotomy on gastric myoelectrical activity: an electrogastrographic study 131
6.3.1. Abstract 131
6.3.2. Introduction 131
6.3.3. Methods 133
6.3.4. Results 136
6.3.5. Discussion 142
6.3.6. References 145
6.4. Gastric myoelectrical activity and solid food emptying following highly selective vagotomy in patients with and without nausea and vomiting 148
6.4.1. Abstract 148
6.4.2. Introduction 148
6.4.3. Methods 150
6.4.4. Results 153
6.4.5. Discussion 157

6.4.6. References 160
6.5. An electrogastrographic study of gastric myoelectrical activity in duodenal ulcer patients 164
6.5.1. Introduction 164
6.5.2. Materials and methods 164
6.5.3. Results 165
6.5.4. Discussion 166
6.6. Gastric myoelectrical activity during the infusion of cis-diamine-dichloroplatinum; an electrogastrographic study 167
6.6.1. Abstract 167
6.6.2. Introduction 167
6.6.3. Methods 169
6.6.4. Results 171
6.6.5. Discussion 174
6.6.6. References 176
7. Summary and conclusions 181
Samenvatting en conclusies 185
References 189
Verantwoording 197
Curriculum vitae 198

List of abbreviations

Ag	silver
CCK	cholecystokinin
Cl	chlorine
cpm	cycles per minute
dB	decibel
DC	direct current
ECA	electrical control activity
EEG	electroencephalography
EGG	electrogastrography
EKG	electrocardiography
ERA	electrical response activity
FFT	fast Fourier transform
GFSD	gastric frequency standard deviation
Hg	mercury
HSV	highly selective vagotomy
Hz	hertz
IF	instability factor
IMC	interdigestive migrating complex
kPa	kilopascal
mV	millivolt
PCV	parietal cell vagotomy
PGV	proximal gastric vagotomy
PR	power ratio
RSA	running spectrum analysis
SD	standard deviation
VIP	vasoactive intestinal peptide

1. Introduction and objectives of the study

Electrogastrography (EGG) is defined as the recording of myoelectrical activity of the smooth muscles of the stomach by means of cutaneous electrodes attached to the epigastric skin. The recorded signal is called an electrogastrogram. The history of electrogastrography is similar to the history of other "EXG" techniques such as electrocardiography (EKG) and electroencephalography (EEG). Pioneering investigators placed cutaneous electrodes near the organ of interest and identified myoelectrical patterns as being typical for certain species under specific conditions. This identification stage of new electrophysiological techniques has always been followed by investigations to determine the relationship between the electrical signal recorded at the surface of the skin and the activity of the organ in question. A third category of study that naturally follows identification and validity is clinical application, some involving normal physiological functioning and others examining the relationship between abnormal myoelectrical patterns of the technique under study and pathology. Although the first electrogastrogram was recorded in 1921 (3) little progress was made with the recording and interpretation of gastric electrical signals until the 1970s. In EKG, which also started in the early 1920s, an enormous increase in knowledge and applicability has been achieved, while in EGG nothing happened until 15 years ago. On the one hand this difference can be explained by the fact that the heart can be considered as a more important organ, and on the other hand the electrogastrogram is much more difficult to record and interpret than EKG. This difficulty arises from the lower frequency content of the electrogastrogram, the many kinds of superimposed noises, the less defined and variable position of the stomach in the body, and the presence of more than one electrical front simultaneously in the stomach. It is not surprising that since the 1970s, with rapidly developing technology, interest in EGG renewed and promising results have been obtained. Research in all three stages, identification, validity, and application, is still being conducted.

In my opinion there is little need for further investigations involving identification and validation of the electrogastrogram. By a thorough comparison of serosal and cutaneous recordings in dogs, Smout (56,57) was able to prove that the myoelectrical activity of the stomach indeed is reflected in the electrogastrogram. His results were in agreement with the work of Nelson and Kohatsu (45) and Brown et al (8). As could be expected, recently Abell et al (1,2) and Hamilton et al (22) came to the same conclusions.

Although the origin of the electrogastrogram is clear, the interpretation of the "raw" electrogastrographic signal is problematic. Visual interpretation is difficult and unreliable. Various signal analysis techniques have therefore been applied. Because the EGG should represent an underlying regular rhythmic process, the method most often used is a frequency analysis (8,33,52,58,70). Almost all authors have used the fast Fourier transform on long stretches of electrogastrographic signal in order to extract the mean gastric frequency. However, in this way time-related information is completely lost. To overcome this problem, van der Schee (75,76) introduced the running spectrum for the analysis of the electrogastrogram. In this technique short overlapping stretches of electrogastrographic time signals are analysed and displayed as a function of time, yielding both time, frequency and amplitude information simultaneously.

The objective of this thesis is to study electrogastrographically the gastric myoelectrical behaviour in both healthy subjects and in patients, to investigate whether EGG can contribute to the understanding of the relationship between gastric myoelectrical activity and disease.

Because the interpretation of the electrogastrogram must start from a sound knowledge of the processes taking place on the stomach itself, a short description of the physiology of the stomach is given in chapter 2. Following a short literature survey, in chapter

3, the recording and signal analysis techniques and the accuracy and reliability of the method are discussed in chapter 4. The results in healthy subjects are summarized in chapter 5. The studies in several patient groups form the subsequent chapter. In the last chapter the results and implications are discussed.

2. Physiology of the stomach

2.1 Introduction

The main physiological function of the stomach is processing food in such a way that, after the ingestion of a meal, small portions of partially digested chyme are intermittently propelled into the small bowel. This function is associated with complex motility patterns. Contractions of the smooth muscles of the muscularis externa are regulated to produce four responses. 1) After the ingestion of a meal, the muscles of certain regions of the stomach relaxes to accommodate the meal. 2) During digestion of the meal, gastric contractions mix the meal. 3) During digestion of the meal, gastric contractions are co-ordinated with motor activity of the pylorus and upper small intestine so that gastric contents are emptied into the duodenum in a regulated and orderly manner. 4) During the interdigestive state, forceful, periodic contractions sweep all remaining gastric contents into the duodenum.

2.2 Anatomical considerations

As far as motility functions of the stomach are concerned, the organ can be divided into two major areas. The proximal region includes the fundus and a part of the corpus. The muscles of this region exhibits mainly tonic activity and allows for rather large changes in intragastric volume with little increase in intragastric pressure. The distal region includes the antrum and a part of the adjoining corpus. Contractions in this region are more phasic in nature. The contractile activities of both regions are co-ordinated by various controlling mechanisms.

Smooth muscle cells of the muscularis externa of the stomach are arranged in three layers: an outer longitudinal layer, a middle circular layer and an inner oblique layer (31). The circular and longitudinal muscle layers become thicker towards the duodenum thus forming the pylorus.

The stomach is richly innervated with both intrinsic and extrinsic nerves (18).

The intrinsic nerve cell bodies lie in two nerve nets which completely envelop the gut between the longitudinal and circular muscle layers (the myenteric plexus, the most prominent) and between the circular muscle and submucosa (Meissner's plexus). The nerve cells synapse with nerve endings from other intrinsic neurones in the plexus as well as with endings of extrinsic nerves. Many neural and paracrine transmitters are found in these cell bodies and nerve endings of the enteric plexus and they probably play an important physiological role (11,15,18,24).

Extrinsically, the stomach is innervated by branches of the vagus nerves and by fibers originating in or passing through the coeliac plexus (18). Many fibers in the vagus are afferents which project from receptors in the stomach. Receptors have been identified that discharge in response to antral contractions (5) and to distension of the stomach (47). Vagal efferent fibers are of two main types: cholinergic stimulatory and non-adrenergic inhibitory. The sympathetic fibers from the coeliac plexus are both afferent and efferent. The afferent fibres arise from receptors in the stomach and synapse either within the coeliac ganglion or in the spinal cord. The efferent fibres are primarily postganglionic adrenergic and synapse mainly with neurones of the intrinsic plexuses.

2.3 Myoelectrical properties of gastric smooth muscle

The underlying control mechanism of motility is of electrical nature and is based on the electrical behaviour of the smooth muscle cells. There is a marked difference in intrinsic behaviours of the smooth muscle cells from the two regions in the stomach (68).

Gastric smooth muscle cells from the oral region have resting membrane potentials of around -50 mV and there are no spontaneous fluctuations in their potentials, but both hyperpolarization and depolarization can be induced. Microelectrodes inserted into gastric smooth muscle cells demonstrate a gradation of the resting membrane potential from fundus to antrum with the former being approximately 20 mV less negative than the latter (68). The importance of these observations become apparent when the relationship between resting membrane potential and tension generated by smooth muscle cells is considered. The fundic smooth muscle cells at their resting membrane potential are partially contracted. Thus, hyperpolarization of these cells will allow the muscle to relax and thereby increase the volume of this region. This is not the case in the antrum, where the muscle is fully relaxed at the resting membrane potential and therefore will not relax further when hyperpolarized.

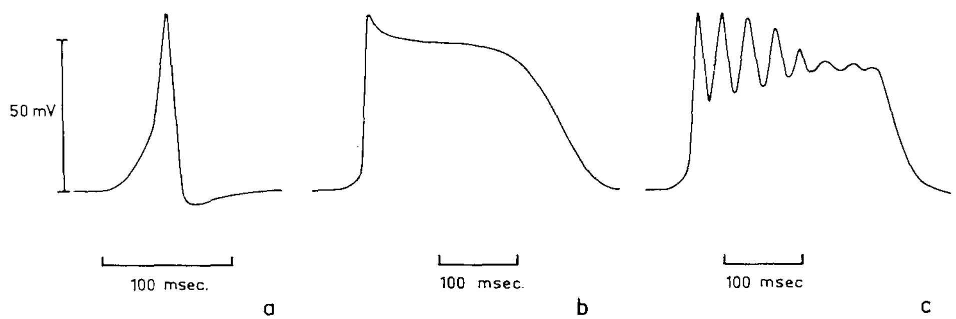


Fig. 2.1 Configuration of the action potentials generated by gastric smooth muscle cells. a) not contraction-related, no plateau-phase present; b) contraction-related, plateau-phase present; c) contraction-related, plateau-phase with spikes.

Muscle cells from the aboral part of the stomach generate spontaneous fluctuations in membrane potential (16). These depolarizations and repolarizations begin from a resting potential of -70 to -50 mV, depending of the gastric region. In some respects, the potentials resemble those seen in the conducting tissue and muscle of the heart. Muscle cells from most areas of the stomach show an initial rapid depolarization and repolarization which is then followed by a more prolonged depolarization or plateau which in turn is followed by repolarization (fig. 2.1). A contraction can be initiated during the plateau phase. When a contraction occurs the duration of the plateau phase is longer and fast pulse like potential changes (spikes) may be superimposed (fig. 2.1). Although these spontaneous potential changes can be recorded from isolated segments of muscle from all areas of the aboral region of the stomach, their intrinsic repetition frequencies differ. The highest frequencies are recorded from cells of the mid stomach near the greater curvature. Frequencies are progressively lower for cells from nearer the pylorus and the lesser curvature. This gradient in frequency can not be found in the intact stomach since all areas influence each other.

The cells with the highest frequency, situated along the greater curvature in the oral part of the corpus, overrule cells with a lower frequency so that with extracellular electrodes a single frequency is recorded (81). Thus, like the heart, the stomach may be considered to have a pacemaker. Many names have been given to this periodic potential change. In this thesis we will use the term Electrical Control Potential (ECA) (51). The specific potential changes when contractions occur will be called Electrical Response Activity (ERA) (51). In man the interval duration between successive ECAs is in the order of 20 seconds, corresponding to a repetition frequency of about 0.05 Hz (3 cpm). The amplitude of the ECA, when measured monopolarly with an extracellular electrode, is in the order of 1 mV in the corpus and 3 mV in the antrum (23,30). The ECA generated in the pacemaker area travels aborally through the longitudinal muscle fibers to the pylorus where it vanishes. The propagation velocity increases towards the pylorus from 0.3 cm/s in the corpus to 1 cm/s in the aboral antrum (23), so that 2 or 3 ECA fronts are simultaneously present on the stomach. It must be emphasized that, unlike the heart, ECA is not always accompanied by contractile activity. When contractions do occur, ECA is followed by ERA.

In summary, two kinds of electrical activity can be distinguished in the extracellular signal: 1) ECA, an always present, periodic activity not indicative of contractile activity. 2) ERA, time-locked to the ECA, only occurring in connection with phasic contractile activity.

2.4 Normal patterns of gastric motility

In the interdigestive phase, the stomach is mechanically inactive during considerable periods of time, and only ECA fronts are propagated aborally. In 1969, Szurszewski reported recurring fronts of ECA followed by ERA in the small intestine of fasting dogs (66), which migrated slowly down the entire small bowel. After reaching the terminal ileum, a new front developed in the duodenum. In 1975, Code and Marlett observed that this so called Interdigestive Migrating Complex (IMC) also occurred in the stomach (10). They defined four phases in each cycle of the electrical complex. Phase I of the complex was characterized by the relative absence of ERA. Persisting but random ERA associated with at least 10% of the ECA was identified as phase II. Phase III was defined as the sudden onset and continuous occurrence ERA with every ECA. Phase IV was characterized by rapid decrease in incidence (to less then 10%) of ERA. The motor correlate of the IMC has been described in dog by Itoh et al (28). The four sequential phases (I-IV) correspond to motor quiescence (phase I), preceeding irregular contractions (phase II), strong regular contractions (phase III) and subsiding contractions (phase IV), as is shown in fig. 2.2. Interdigestive motor activity in man has mainly been studied manometrically (34,77,78). The human IMC pattern resembles that of dogs, although it seems to be somewhat less constant with regard to periodicity and site of origin (78). Functionally, the IMC may be considered to act as a gastrointestinal housekeeper, periodically sweeping the small bowel clean (9). Bacterial overgrowth in the small intestine has been reported in patients in whom the motor activity front of the IMC was absent (78).

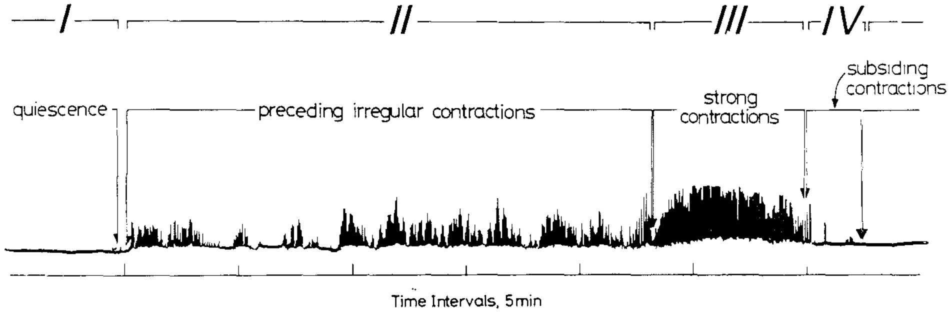


Fig. 2.2 Comparison of nomenclature of the interdigestive migrating complex in canine jejunum.

After ingestion of a meal, the interdigestive pattern is interrupted not only in the stomach but, simultaneously, in the entire intestine. The duration of this interruption depends on the volume and physicochemical composition of the meal (50). The postprandial gastric motor pattern is characterized by the continuous occurrence of contractions and of course their electrical correlate, i.e. ECA accompanied by ERA. In man, immediately after food intake, the repetition frequency of the ECA decreases, followed after about 10 minutes by an increase in frequency to equal or above the fasting level (14). The motor correlate of this phenomenon is still unknown.

2.5 Control mechanisms of gastric motility

There are three main factors controlling gastric motility and emptying: 1) Composition and physicochemical properties of the meal. 2) Neural control. 3) Hormonal control.

Composition and physicochemical properties of a meal are important in determine the motility pattern of the stomach. The liquid phase of any meal appears to empty from the stomach in an exponential manner, probably as a result of low amplitude tonic contractions initiated in the fundus. On the other hand, antropyloric co-ordinated motor activity producing high amplitude (>100 mmHg) phasic pressure changes and rapid flow currents in the antrum are necessary to grind solids down by liquid shearing to particles of less than 1 mm diameter (42). This allows solids to be suspended and emptied from the stomach with the bulk of the liquid phase of a meal. Non-digestible solids cannot be ground in this manner, and therefore leave the stomach slowly. Large particles that cannot be reduced in size are emptied during phase III of the interdigestive migrating complex. Thus, emptying is proportional to the square root of the volume (25). However, other physicochemical properties of the meal influence gastric emptying. Increasing osmolality, acidity, and chain length of fatty acids of the meal will delay gastric emptying.

Neural control of gastric motility may be subdivided into: a) Control at electrophysiological cellular level; b) intrinsic control by the enteric nervous system; and c) extrinsic control by the autonomic nervous system. In b) and c) a neural as well as a humoral component is present.

Electrophysiological control at cellular level depends on the properties of the gastric smooth muscle cells in different parts of the stomach as is discussed in chapter 2.3.

The intrinsic nerves of the stomach have received little study, although the myenteric plexus is abundant in the stomach, in particularly in the pyloric region. Most studies on intrinsic nerves have been on preparations of small bowel. Such studies have demonstrated that VIP-containing neurones appear to project in an aboral direction so that neurones at on level innervate the muscle aborally. Since VIP inhibits contractions of intestinal smooth muscle, such nerves may be responsible for the phase of descending inhibition of the peristaltic reflex. Whether such pathways are present in the stomach remains to be solved (17). Another interesting aspect is that following bilateral section of the thoracic vagus the ECA and ensuing motility is disorganized but returns to normal after several weeks, presumably because of adaptive changes in the enteric plexus (6). The intrinsic innervation seems to be a necessity for the initiation and propagation of the IMC (83-85).

Extrinsic nerves exert a major influence on gastric motility and many reflex pathways in the stomach rely on the extrinsic nerves. The major inhibitory influence to the stomach is vagal and via a non-adrenergic, non-cholinergic transmitter. This pathway is activated by e.g. swallowing, sham feeding. The effects of vagotomy have been recognized for years. The decrease in gastric contractions, in gastric distensibility, and in gastric emptying of solids and semi-solids are due to the loss of extrinsic cholinergic stimulatory and non-adrenergic inhibitory innervation. Stimulation of the central nervous system, e.g. by chemicals or labyrinthine stimulation, elapse via extrinsic neural pathways (69). There is also evidence that the amplitude and even the waveform of gastric ECA depends on extrinsic influences (21,67). Interesting is also the finding that distension of the corpus stimulates antral contractions via a cholinergic pathway. This so called corpo-antral reflex occurs even when the stomach is divided across the incisura and is abolished by vagotomy (4). The increase is proportional to the degree of corpus distension. Inhibition of antral motility can elapse via both vagal- and splanchnic pathways. Besides the hormonal control, the extrinsic nerves play a role in the occurrence of gastric IMCs since vagotomy disrupts IMCs in the caudal stomach, but not in the rest of the small bowel (83,84).

Studying hormonal control of gastric motility is not easy, because it is difficult to determine whether any of these agents acts physiologically. Most of the endocrine and paracrine chemicals found in the gut affect gastric contractile activity. Infusion of gastrin, CCK, secretin, VIP and several other peptides alter receptive relaxation, gastric tone and antral contractions. Motilin is presumably of importance in the occurrence of gastric IMCs (48,79).

3. Literature survey

Although the term electrogastrography has occasionally been used for serosal and/or mucosal recordings of gastric myoelectrical potentials, this survey is limited to publications dealing with cutaneous recordings in man. Only those papers important for the general development of EGG will be mentioned. Publications concerning the more specific aspects of the gastric myoelectrical activity and the corresponding EGG findings in healthy subjects and in patients will be discussed in the following chapters.

The first human electrogastrogram was recorded in 1921 by Alvarez (3) in an elderly woman with a hernia of the abdominal wall which was so thin that Alvarez could observe gastric contractions with a frequency of 3 cycles per minute, that corresponded to sinusoidal waves with the same frequency appearing in the electrogastrogram.

The second group of investigators who identified the electrogastrogram were the pediatricians Tumpeer, Blitzsten and Phillips (73,74). These authors also correlated visible gastric peristalsis with the electrogastrogram. They also mentioned that cardiologists often noted a changing baseline that could not be explained for in terms of known responses of the cardiovascular system. Tumpeer assumed that these were due to the gastric myoelectrical activity. Thus, gastric myoelectrical activity has been recorded, but perhaps not recognized as such, since the time of the first ECG at the beginning of this century. Nowadays the 3 cycles per minute baseline variations are not observed in the ECG because the low frequencies are filtered out.

No papers dealing with electrogastrography could be traced until 1953. In that year Ingrams and Richards (27) described the results of EGG in 45 subjects. Analysis was performed by visual inspection. Results were not provided but summarized in a rather cryptic sentence: 'Movement of the wakeful patient was obviously a factor, for a skin/skin tracing from a sleeping subject became completely flat ....'.

In the late fifties Davis, a physiological psychologist, began a series of exploratory studies with EGG. Davis et al (12,13) found potential variations with a frequency of about 3 cycles per minute (cpm) and amplitudes in the order of 100-500 mV. The initial study also included an attempt to validate EGG using concomitant recordings from a mine detector that picked up the movements of a steel ball in the stomach. It was concluded that: 'There is little doubt that we show an electrical aspect of the ordinary gastric or enteric contractions of three to four per minute'. These authors were primarily interested in the response to psychological stimuli.

In 1959 Tiemann and Reichertz published two papers (71,72) on what they referred to as the electrointestinogram. The authors reported that, in agreement with earlier investigators, they found a frequency of 3 cpm when recording the electrogastrogram in normal resting subjects.

Several reports have appeared in the Russian literature starting with a paper by Sobakin and Mishin in 1958 (60). An important early EGG paper in Russian was written by Krasil'nikov (32), who compared recordings of normals with individuals suffering from various disorders of the gastrointestinal system. Sobakin, Smirnov and Mishin (61) reported that they compared the electrogastrograms in the postprandial state from 61 healthy subjects and 164 patients suffering from various gastric disorders. They found normal myoelectrical activity in patients with gastric ulceration along the lesser curvature. In patients with a pyloric stenosis the amplitude of the gastric waves was increased to twice that of normal subjects. In patients with gastric carcinoma, waves with a highly variable rhythm and low amplitude were observed. Their final conclusions were: 'Clinical approbation of the electrogastrographic method and equipment discussed here has shown it to be completely suitable for objective pathophysiological studies of the displacements of the motor system of the stomach during digestion'.

During the mid-1960s Stern published 3 papers (62-64) dealing with the effects of various forms of sensory stimulation on the electrogastrogram.

Since 1967 Martin and his collegues in Tours, France, have published numerous papers dealing with the use of EGG to study gastric activity in both healthy and diseased states (36-41). The authors were of the opinion that signals recorded from the skin reflect contractile activities and that absence of visually recognizable waves implies absence of contractile activity. However, experimental confirmation was not provided.

Up until the mid-1960s, and the French group until the late 1970s, investigators who used EGG assumed that they were recording from the surface of the skin potential changes that were due to the contractions of the smooth muscles of the stomach; that is, they assumed a one-to-one relationship between the electrogastrogram and the contractions of the stomach. In 1968 Nelson and Kohatsu (45) presented a different view of the source of the EGG signal. They stated that the electrogastrogram was a function of gastric slow wave activity, pacemaker potential, or electrical control activity (ECA) (synonymous terms). Furthermore they presented evidence that indicated that when contractions do occur they are time-locked to the ECA and, therefore, to the EGG.

Beginning in 1975 Duthie and his colleagues in Sheffield, England, published a few studies (8,14) in which they examined the dominant frequency of the electrogastrogram and made technical advances in the analysis of the EGG signal because visual analysis turned out to be unreliable. In one of their studies (8) the Sheffield group compared the EGG signal with intragastric pressure recordings. Their findings were the same as those of Nelson and Kohatsu (45). When contractions occurred they occurred at the same frequency as the dominant frequency in the EGG signal; and, whereas the electrogastrogram showed 3 cpm almost continuously for most subjects, contractions as recorded with intragastric pressure instruments did not. After food intake they found an 2.5-fold increased amplitude of the dominant, gastric, frequency in the EGG signal, which they attributed to a decreased distance of the electrodes to the distended stomach. Smallwood (53), one of the investigators of this group, studied both healthy subjects and patient groups. In 14 healthy volunteers he found with EGG a mean fasting gastric frequency of 3.02 ± 0.21 cpm and a mean postprandial gastric frequency of 3.09 ± 0.27 cpm. Immediately following the meal a significant frequency drop was found. In another group of normal subjects a significantly different postprandial frequency (3.30 ± 0.25 cpm) was found. Smallwood suggested that this difference was due to the different age distributions of the 2 groups; the first group consisted of volunteers of 21 to 33 years of age, whereas the second group covered a much wider span of years. In patients before and after truncal vagotomy and pyloroplasty a significant increase in mean gastric frequencies was reported (from 3.15 ± 0.24 to 3.44 ± 0.27 cpm).

From 1980 to the present, evidence has been provided that the EGG signal provides not only information about frequency of the ECA but, indeed, that the amplitude of the EGG is very much related to the presence or absence of contractions. Important publications in this new era of EGG interpretation were the thesis of Smout (56) and other publications (57-59) from the Dept. of Medical Technology, Erasmus University in Rotterdam, The Netherlands, where he worked with van der Schee and Grashuis. They concluded that the ECA and the, contraction related, electrical response activity (ERA, a second potential with or without superimposed fast oscillating potential changes) are reflected in the electrogastrogram.

Another important contribution of this group was the introduction of running spectrum analysis in the field of EGG (75,76). In this technique, using the fast Fourier transform, power spectra of short, overlapping stretches of EGG time signals are computed and displayed as a function of time, yielding both time, frequency and amplitude information simultaneously.

Despite the progress made, EGG has a relatively short history compared to ECG and EEG and, therefore, research concerned with its identification and validation continues to be necessary even as investigators apply it to the study of gastric motility in health and disease.

4. Electrogastrography

4.1 Introduction

When judged by the amplitude of the generated potentials the stomach is the most electrically active internal organ after the heart. Analogous to the terms electrocardiography (EKG) and electroencephalography (EEG) the term electrogastrography (EGG) has been used for the method of recording gastric myoelectrical activity by means cutaneous electrodes. In the sections 4.2 and 4.3 the electrogastrographic recording and signal analysis techniques used in our studies will be described. In the section 4.5 the accuracy and reliability of electrogastrography are evaluated.

4.2 Technique of recording

In electrogastrography, as in other "EXG" techniques, electrodes are attached to the skin. The signals picked up by the electrodes have to be amplified and filtered in order to reduce or eliminate disturbing signal components. The technique of EGG appears to be simple. However, the fundamental frequency of the signal is very low (the repetition frequency of gastric ECA is 0.05 Hz in man). Since both electrode noise and electrode impedance increase with decreasing signal frequency (19) it is important to select the most appropriate type of electrode for electrogastrographic purposes. With respect to noise, impedance and sensivity for motion artefacts, it has been found that commercially available EKG electrodes, particularly the pre-gelled Ag/AgCl electrodes of the recessed type (i.e. the metal of the electrodes is built in a small basin filled with a gel-containing sponge) are adequate (56,76).

Electrogastrographic signals can be recorded from electrodes attached to the limbs, but the signals with the best signal to noise ratio are those obtained from electrodes placed on the upper abdomen. Bipolar recording (potential differences between two electrodes on the abdomen) yields "cleaner" signals than monopolar (one electrode on the abdomen and one on a limb) (53).

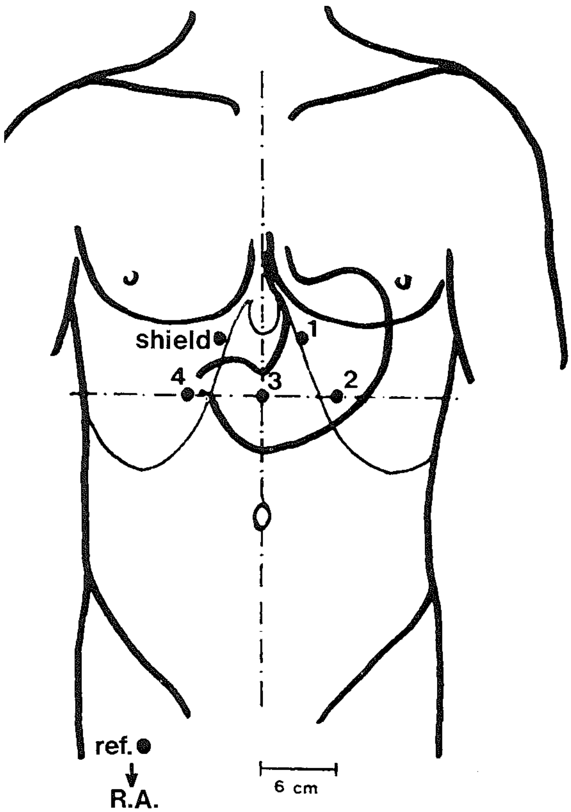


fig. 4.1 The electrode positions used in our studies. Electrodes 2,3, and 4 are situated on a transverse line halfway between the lower end of the sternum and the umbilicus. Electrode 3 is placed at the intersection of this line and the median plane. Distance between all abdominal electrodes is 6 cm. Reference electrode is on the right ankle (RA).

However, if the shape of the signals is to be studied, monopolar signals must be used, and we therefore record both bipolar and monopolar abdominal signals.

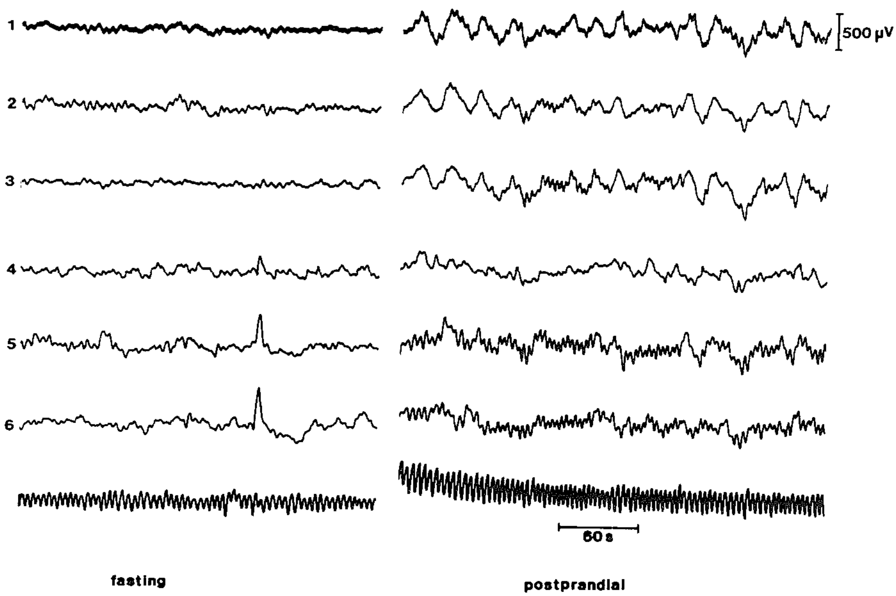


fig. 4.2 Electrogastrogram recorded in a healthy subject. Six monopolar signals are shown, 4 min in the fasting state and 5 min in the postprandial state. Note the postprandial amplitude increase.

Although in most subjects an optimal electrode direction coincides with the antral axis (43), a universal optimum electrode position cannot be defined exactly because of inter-individual anatomical variations (20,59). We therefore use several leads and the signal with the best signal to noise ratio is then selected for further analysis. In this choice, contamination of the signal with a respiration component, which has a different frequency range, is of less importance than are large motion artefacts, which occur in particular in the monopolar leads. The positions of the 6 recessed-type electrodes (Red Dot 2256, 3M Co.) used in this study are shown in fig. 4.1. The shield electrode is used to reduce possible interference from the 50 Hz mains voltage at the input stage of the preamplifiers. A strain gauge respiration transducer is attached to the thoracic wall. The 4 monopolar and 6 bipolar signals are recorded on paper (Van Gogh EP-8b) and simultaneously stored on magnetic tape (Racall Store 14). In fig. 4.2 six monopolar cutaneous signals are shown of a healthy subject.

In order to avoid attenuation of the EGG signal, and to minimize noise, the band width of the amplifier should be chosen with care. Cut-off frequencies of 0.01 Hz and 0.50 Hz for the high- and low-pass filters respectively (6 dB/octave) have been found to be suitable (75,76).

4.3 Signal analysis and data presentation

As previously mentioned, visual interpretation of the electrogastrogram is difficult and does not give adequate information. Various signal analysis techniques have therefore been applied to electrogastrographic signals. The method most often used is a frequency analysis based on Fourier analysis because abnormal myoelectrical activity seems to be characterized predominantly by abnormal gastric ECA repetition frequencies. In the past most authors used the fast Fourier transform on long stretches of electrogastrographic signal in order to extract the mean gastric frequency in those long stretches (8,33,52,58,70). However, in this way information on changes in frequency during the recording session is completely lost. To overcome this problem van der Schee et al (75,76) used running spectrum analysis (RSA). In this technique, using the fast Fourier transform, power spectra of short, overlapping stretches of electrogastrographic time signals are computed and displayed as a function of time (fig. 4.3). RSA thus provides both time and frequency information simultaneously. In addition the power content of the gastric frequency is a measure for the amplitude of the electrogastrogram.

The fast Fourier transform algorithm is implemented on a NOVA 2 digital computer. The signals, replayed from tape 16 times faster than real time, are preprocessed by band-pass filtering using a butterworth filter (24 dB/octave) with (real time) cut-off frequencies set at 0.01 and 0.5 Hz, to remove possible DC components and to avoid aliasing (75,76). They are then digitized (real time sampling frequency 1 Hz) and fed into the computer.

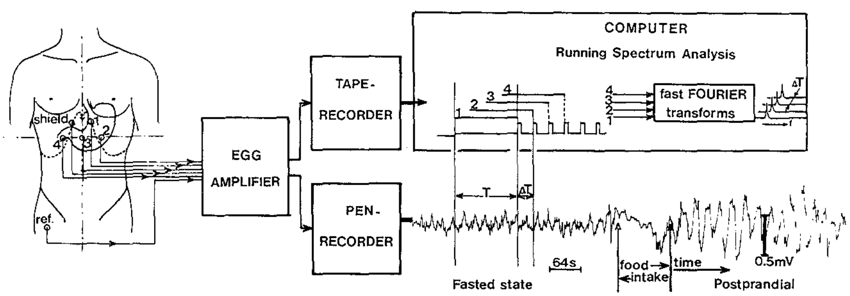


fig. 4.3 Schematic presentation of the principle of running spectrum analysis.

Spectra are obtained as follows: every 64 s a power spectrum is computed from the preceeding 256 s of the EGG time-signal, to which a Hamming window has been applied to reduce leakage (7). These time values have been shown to enable the extraction of relevant information from the EGG, giving 129 points per spectrum and a frequency spacing of 0.0039 Hz (75,76). During processing each computed spectrum is drawn, with its spectrum number, on a Tektronix 4010 display terminal with hard copy facilities. A pulse train is echoed from the computer by a digital-to-analog converter and also recorded on paper together with the analog input signal. The distance between these pulses indicates the time shift of the computed spectra. In this way the time signal corresponding to a particular spectrum can be established exactly. Thus, each individual spectrum can be analysed in detail if interpretation problems occurred after completion of the processing.

This procedure generates a series of overlapping spectra, called running spectra. Computer programs enable two different graphical representations of these spectra. In fig. 4.4 the spectra are displayed as a pseudo-3-dimensional plot. Such a display can be rotated in order to change the viewing angle.

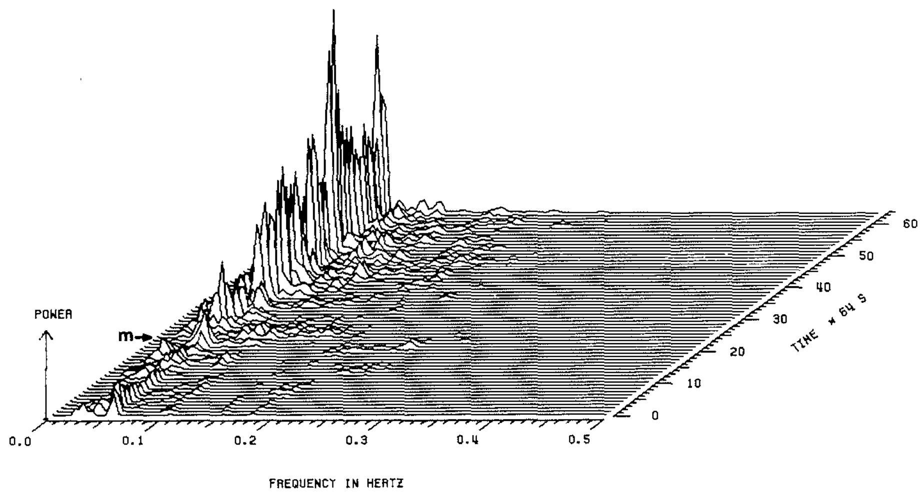


fig. 4.4 Pseudo-3-D display of the electrogastrogram partly shown in fig. 4.2. Note the power increase of the gastric ECA frequency, visible at about 0.050 Hz, after the test meal marked with 'M'.

The data can also be displayed as a grey-scale plots (fig. 4.5): each point in the (frequency, time) plane is represented by a picture element (pixel), the blackness of which is proportional to the magnitude of power. The grey resolution is bounded by 16 distinct grey levels. The grey-scale plot, in particular, facilitates recognition of frequency patterns. Relative power changes can be recognized more precisely in the pseudo-3-dimensional plot. Plots are made on a Versatec 1100 A printer/plotter.

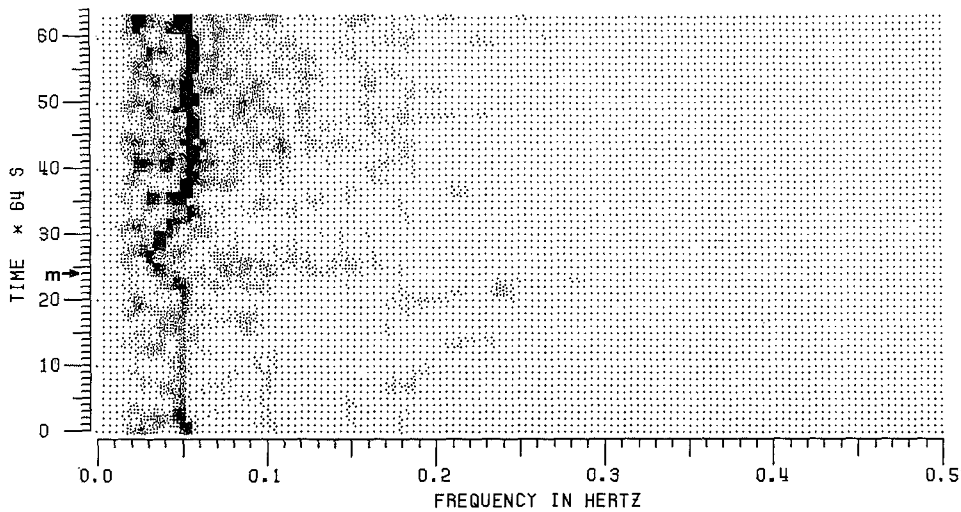


fig. 4.5 The grey-scale plot of the electrogastrogram partly shown in fig. 4.2. Note the frequency decrease following the test meal marked with 'M'. The postprandial power increase is expressed by the increased blackness.

In addition the mean (dominant) frequency (Hz) with standard deviation (SD) of the gastric signal and its power content can be computed from the mean of a series of spectra, e.g. for the fasting and postprandial states (Fig. 4.6 and 4.7).

The SD obtained from this mean spectrum can be used as a measure for the long-term stability of the gastric frequency. The larger the SD, the more unstable is the gastric frequency in the analysed period. However, the SD of the mean frequency fails to provide an indication of all the frequency variations visible in the grey-scale plot (e.g. fig. 4.6). Due to short-term frequency instability, large frequency variations can occur within 1 spectrum (256 s). To discriminate between the short-term and long-term instability of the gastric frequency the Instability Factor (IF) is introduced.

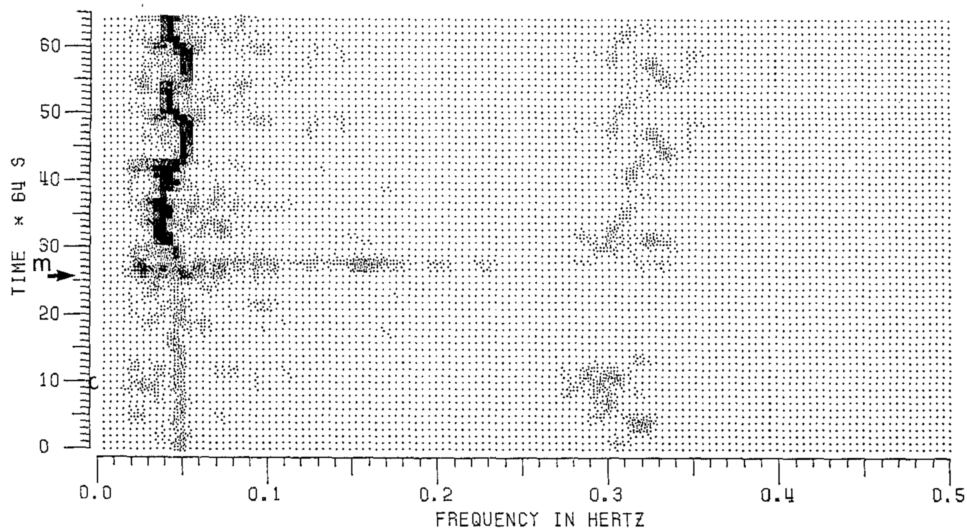
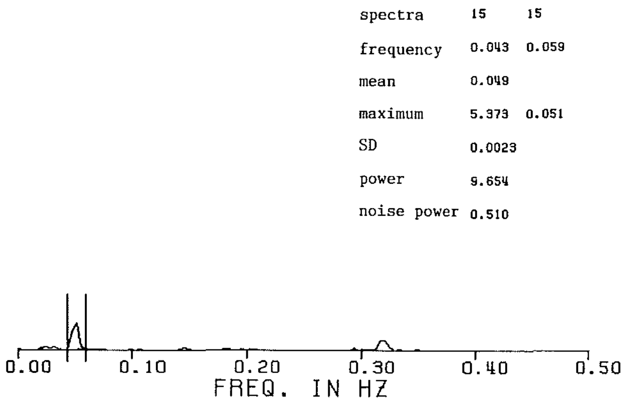
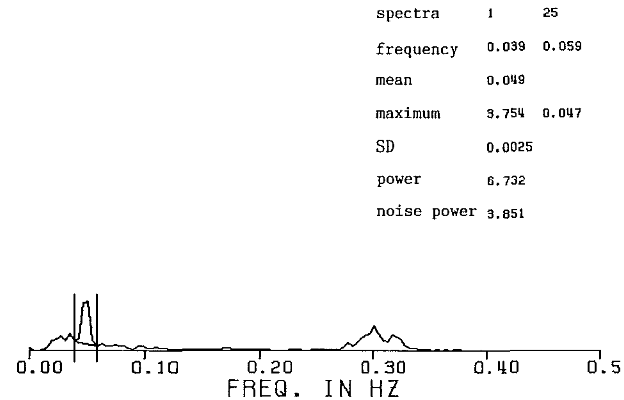


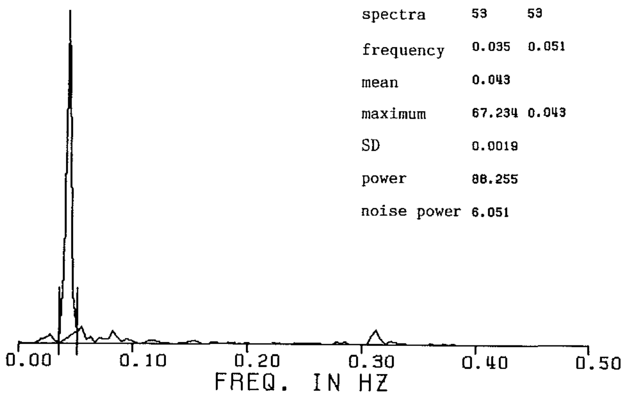
fig. 4.6 The grey-scale plot of an electrogastrogram of a patient with nausea and vomiting. In the fasting state a stable gastric ECA frequency is seen at about 0.050 Hz. After the test meal marked with 'M' a normal power increase is seen but the frequency is very unstable.

This parameter is defined as the ratio of the frequency standard deviation of the mean of a series of spectra (e.g. the whole fasting or postprandial period) to the frequency SD of one, arbitrary choosen, representative spectrum (containing a clearly present gastric frequency component) of this series (fig. 4.7 and 4.8).

Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content, the amplitude is the square root of the power) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance to the stomach wall) it is impossible to make a comparison of inter-individual and even intra-individual power data (in separate recording sessions).


spectra 15 15
frequency 0.043 0.059
mean 0.049
maximum 5.373 0.051
SD 0.0023
power 9.654
noise power 0.510
0.00 0.10 0.20 0.30 0.40 0.50
FREQ. IN HZ


spectra 1 25
frequency 0.039 0.059
mean 0.049
maximum 3.754 0.047
SD 0.0025
power 6.732
noise power 3.851
0.00 0.10 0.20 0.30 0.40 0.50
FREQ. IN HZ


spectra 53 53
frequency 0.035 0.051
mean 0.043
maximum 67.234 0.043
SD 0.0019
power 88.255
noise power 6.051
0.00 0.10 0.20 0.30 0.40 0.50
FREQ. IN HZ

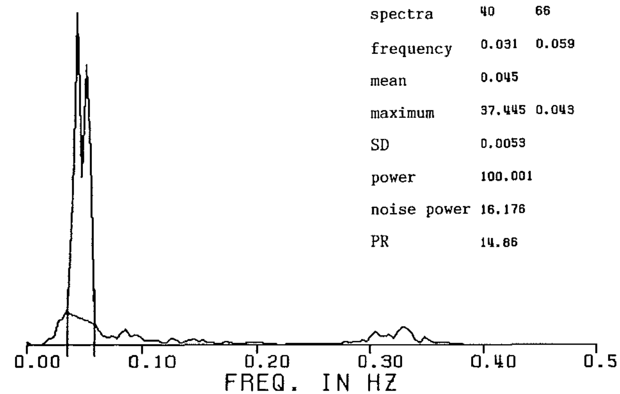

spectra 40 66
frequency 0.031 0.059
mean 0.045
maximum 37.445 0.043
SD 0.0053
power 100.001
noise power 16.176
PR 14.86
0.00 0.10 0.20 0.30 0.40 0.50
FREQ. IN HZ

fig. 4.7 Mean spectra (with the computed values for mean frequency, SD and power) of 25 fasting spectra (1-25) and of 27 spectra in the postprandial state (40-66) of the electrogastrogram shown in fig. 4.6.

fig. 4.8 Spectrum number 15 in the fasting state and spectrum number 53 in the postprandial state (with computed values for mean frequency, SD and power) of the electrogastrogram shown in fig. 4.6.

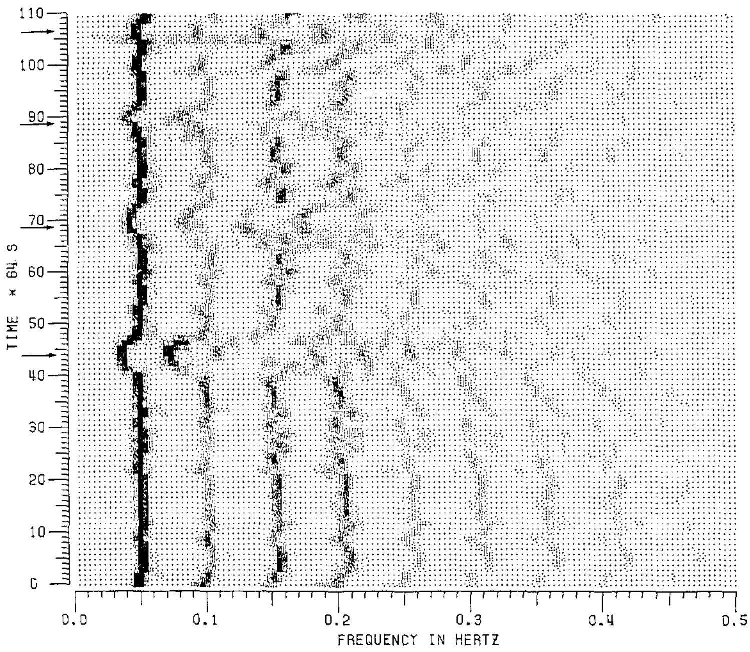


fig. 4.9 The grey-scale plot of a human serosal signal (electrodes on the gastric antrum) clearly showing multiple higher harmonics (0.10, 0.15, 2.0, 2,50 Hz etc) of the gastric ECA frequency at 0.050 Hz. The large number of higher harmonics is due to the waveform of the serosal signal.

In this study only power changes in one single recording session are used for analysis. To quantify the postprandial power change, the ratio of the power of the mean spectrum of the postprandial state to the power of the mean of the fasting state is computed and referred to as the Power Ratio (PR) (fig. 4.7).

Where necessary running spectrum analysis of the respiration signal is performed to exclude confusion between frequencies of respiratory origin and possible tachygastrias.

The only parameter associated with the electrogastrographic waveform that is used in this study is the presence of a second harmonic in the spectrum. Higher harmonics can be recognized in the spectrum because their frequency is exactly an integer multiple of the basic frequency (fig. 4.9). The more a periodic signal deviates from a sinusoid, the more harmonics may be expected to be present. A second harmonic of the gastric frequency is considered to be present if its power amounted to at least 5% of the power of the first harmonic, i.e. the gastric frequency itself.

4.4 Standard recording procedure

Myoelectrical activity during fasting was recorded for a 30 min period after an overnight fast. A test meal consisting of 250 ml of yoghurt with 20 g of sugar was then given, and consumed within 4 min, while the recording was continued. The composition of the test meal was: 990 kJ, 8.75 g protein, 8.75 g fat and 30 g carbohydrate. The recording was stopped 35 min after the start of the test meal. Subjects lay quietly in a supine position during most of the recording session, only sitting up while taking the test meal.

4.5 ACCURACY AND RELIABILITY OF ELECTROGASTROGRAPHY

Submitted for publication.
Co-authors E.J. van der Schee, J.L. Grashuis.

4.5.1 Abstract

Electrogastrography (EGG), the recording of gastric myoelectrical activity using cutaneous electrodes is a new technique, it is therefore necessary to evaluate its accuracy and reliability. Its accuracy was evaluated by comparing the electrogastrogram with gastric myoelectrical activity recorded by serosal electrodes. Its reliability was evaluated by comparing a series of electrogastrograms measured at intervals in healthy subjects. Conclusions: 1) the fundamental frequency in the electrogastrogram is of gastric origin and is equal to the repetition frequency of the gastric ECA; 2) electrogastrography gives a reliable way of measuring the gastric frequency and its frequency variations; 3) in the present form, with 30 minutes recording in the fasting state, the quantification of the postprandial amplitude increase of the gastric frequency in the electrogastrogram, indicative of gastric motor activity, is less reliable due to the motor activity of the interdigestive migrating complex.

4.5.2 Introduction

Electrogastrography (EGG), the recording of gastric myoelectrical activity using cutaneous electrodes, has yet to achieve widespread recognition as a clinical or research tool in gastroenterology, despite the fact that the first electrogastrogram was recorded 60 years ago. However, since the 1970s interest in this topic has increased, due to the recognition of the fact that the myoelectrical activity of the stomach plays an important role in controlling motor activity.

The stomach has an inherent rhythmic myoelectrical activity with a repetition frequency of 0.05 Hz (3 cpm), which is referred to as electrical control activity (ECA) (1,2). When motor activity is present, the ECA is accompanied by a second component, with or without superimposed fast oscillating potential changes (spikes or spike activity), referred to as electrical response activity (ERA) (2).

By a thorough comparison of serosal and cutaneous recordings in dogs, Smout et al (3) were able to show that gastric myoelectrical activity is reflected in the electrogastrogram. Their results were confirmed by those found by other authors in dogs and, despite the limited amount of data, in man (4,5).

Interpretation of the electrogastrogram, however, remains a problem and this is perhaps the reason why little progress has been made in past decades. Visual analysis is unreliable and much of the information present in the electrogastrogram cannot be discerned because motion and respiration artefacts. Various techniques of signal analysis, in particular frequency analysis, have been applied. In most techniques time information is lost. To overcome this problem van der Schee et al (6) introduced running spectrum analysis of the electrogastrogram. In this technique, which uses the fast Fourier transform, power spectra of short, overlapping stretches of the cutaneous signals are computed and displayed as a function of time, yielding both time and frequency information simultaneously.

To evaluate the potential applications of EGG more needs to be known about 1) the accuracy of the procedure, and 2) its reliability. The accuracy of a method is measured by its ability to give the right answer. The reliability, or consistency, of a method is shown by its ability to provide the same answer in repeated observations.

The object of the present study was to evaluate the accuracy of EGG by comparing the electrogastrogram with gastric myoelectrical activity recorded by serosal electrodes. The second objective of the study was to evaluate the reliability of EGG by comparing a series of electrogastrograms measured at intervals in healthy subjects. The serosal recordings and the electrogastrograms were analysed by running spectrum analysis.

4.5.3 Materials and methods

Technique of recording.

In the first part of the study (to test accuracy) three pairs of stainless steel electrodes (separation 5 mm) were attached to the serosal surface of the antrum 1, 3 and 5 cm from the pylorus in a 37-year-old male subject undergoing a cholecystectomy. Each stainless steel wire (diameter 0.15 mm) was stripped of its coating (Trimel, Johnson Matthey Ltd.) over a distance of 6 mm, introduced into the serosa in a transverse direction and fixed with catgut stitches. The wires left the abdomen via a silastic drain. After closure of the wound the 5 cutaneous electrodes (1 shield and 4 recording electrodes, Red Dot 2256, 3M) were attached around the median upper abdominal incision. A reference electrode was placed on the right ankle. A strain gauge respiration transducer was attached to the thoracic wall. Both monopolar and bipolar serosal and cutaneous recordings were made. For the serosal recordings the high- and low-pass filters (6 decibel/octave) were set at 0.012 and 15 Hz respectively. The corresponding values for the cutaneous recordings were 0.012 and 0.5 Hz. All signals were recorded on paper (Van Gogh EP-8b) and simultaneously stored on magnetic tape (Racall Store 14). The recording sessions (duration 2 hours) started 2 hours after the operation and were continued at intervals during the recovery period till the 5th post-operative day, when the drain was removed. Glucagon (0.5 mg) and secretin (80 IU) were given intravenously to induce dysrhythmias. During the recording sessions the subject lay quietly in a supine position.

This part of the study was approved by the Medical Ethics Committee of the Erasmus University, Rotterdam, on September 20, 1982 and a written informed consent was obtained from the subject.

In the second part of the study (to test reliability), gastric myoelectrical activity was recorded using cutaneous electrodes in 12 control subjects (median age 32, range 25-40), who had no history of gastrointestinal or systemic disorder (control group A). There were 4 recording sessions at weekly intervals and measurements were made in both the fasting and postprandial states.

In addition EGG (1 recording session) was performed in 52 subjects (27 men and 25 women, mean age 42, range 16-75), without any history of gastrointestinal or systemic disorder (control group B), to establish the normal values and their ranges in a control population.

The positions of the 6 recessed-type electrodes (Red Dot 2256, 3M Co.) used in this part of the study are shown in fig. 4.5.1. A strain gauge respiration transducer was attached to the thoracic wall. Activity during fasting was recorded for a 30 min period after an overnight fast. A test meal consisting of 250 ml of yoghurt with 20 g of sugar was then given, and consumed within 4 min, while the recording was continued. The composition of the test meal was: 990 kJ, 8.75 g protein, 8.75 g fat and 30 g carbohydrate. The recording was stopped 35 min after the start of the test meal. Subjects lay quietly in a supine position during most of the recording session (only sitting up while eating the test meal). The 4 monopolar and 6 bipolar signals were recorded on paper (Van Gogh EP-8b) and simultaneously stored on magnetic tape (Racall Store 14). The high- and low-pass filters (6 decibel/octave) were set at 0.01 and 0.5 Hz respectively.

This part of the study was approved by the Medical Ethics committee of the Erasmus University, Rotterdam, on June 4th, 1982 and carried out with the informed consent of the subjects.

Signal analysis.

A fast Fourier transform algorithm implemented on a NOVA 2 digital computer was used to obtain the power spectra of the time signals. The leads with the best signal to noise ratio for both serosal and cutaneous time signals were selected for further analysis.

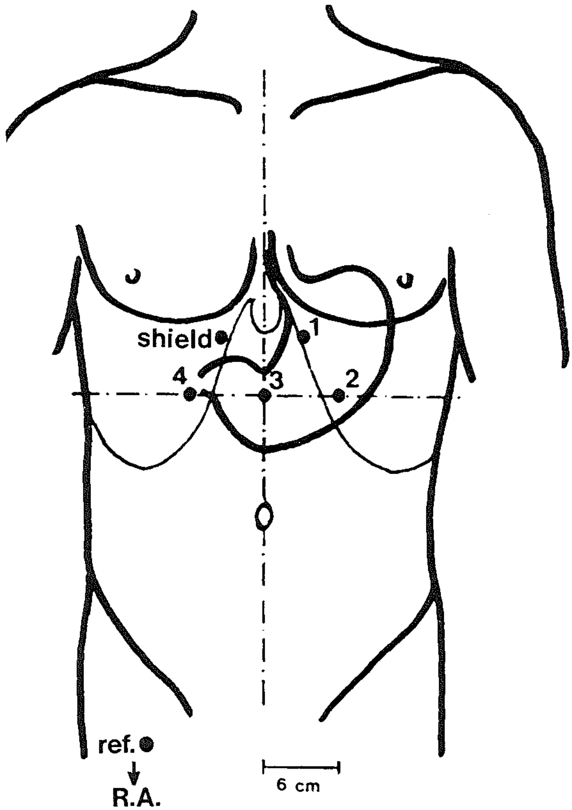


fig. 4.5.1 Positions of the cutaneous electrodes in standard EGG. Electrode 3 is placed at the intersection of a transverse line halfway between the lower end of the sternum and the umbilicus and the median plane. Distance between electrodes is 6 cm. Reference electrode is on the right ankle (RA). The shield electrode was used to reduce the interference from the 50 Hz of the mains voltage at the input stage of the preamplifier.

The signals, replayed from tape 16 times faster than real time, were preprocessed by band-pass filtering using a Butterworth filter (24 decibel/octave) with (real time) cut-off frequencies set at 0.01 and 0.5 Hz, to remove possible DC components and to avoid aliasing. They were then digitized (real time sampling frequency 1 Hz) and fed into the computer. Spectra were obtained as follows: every 64 s a power spectrum was computed from the preceeding 256 s of the EGG time-signal, to which a Hamming window had been applied to reduce leakage (7). These time values have been shown to enable the extraction of relevant information from the EGG, giving 129 points per spectrum and a frequency spacing of 0.0039 Hz (6). Tachygastrias which have a duration of at least 64 s can be detected using these time values (6). This procedure generates a series of overlapping spectra, called running spectra. During processing each computed spectrum was drawn, with its spectrum number, on a Tektronix 4010 display terminal with hard copy facilities. After completion of the processing, a computer program enabled a graphical representation of the spectra. In this study a grey-scale plot was used in which each point in the frequency-time plane is represented by a picture element, the blackness of which is proportional to the the magnitude of power. The 'grey' resolution is limited to 16 distinct grey levels. Plots were made on a Versatec 1100 A printer plotter. This kind of display enables frequency patterns to be easily recognized.

In the first part of the study (testing of accuracy) the recording sessions of 2 hours were divided into periods of 20 minutes. For each of these 20 minutes periods the mean gastric frequency (Hz) and its standard deviation (GFSD) were computed for both the serosal and cutaneous signals. The GFSD was used as a measure for the stability of the gastric frequency. The larger the GFSD the more unstable the frequency, and thus the larger the ECA frequency variations, in the period concerned.

In the second part of the study (testing of reliability) the mean gastric frequency (Hz), its standard deviation (GFSD) and its power content were computed for both the entire fasting period (30 min) and postprandial state (25 min). The postprandial frequency dip was excluded from the calculation of the GFSD.

Motor activity generally manifests itself in the electrogastrogram by an increase in amplitude of the gastric frequency (3,8,9). Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content, the amplitude is the square root of the power) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance from the stomach wall) it is impossible to make a comparison between inter-individual or even between intra-individual power data in a series of recordings. Therefore in this study only power changes in one single recording session were used for analysis. To quantify the postprandial power change as an indication for postprandial gastric motor activity, the ratio of the power in the postprandial state to the power in the fasting state was computed and referred to as the power ratio (PR).

Where it was considered to be necessary, running spectrum analysis of the respiration signal was performed to exclude confusion between frequencies of respiratory origin and possible tachygastrias.

Statistical analysis. To measure the accuracy of EGG (i.e. the ability to provide the right answer) the algebraic difference between the true (serosal) and the observed (cutaneous) values of the mean gastric frequency and GFSD were compared (10). In evaluating the accuracy the frequency variations visible in the grey-scale plots were also used. It was evaluated if the frequency variations visible in the grey-scale plots of the serosal signals were also present in the grey-scale plots of the cutaneous signals.

Measurements should be so reliable that errors induced by the measurement process (EGG) do not significantly widen the range of values for the normal population. According to Barnett (11), this objective is achieved by methods whose standard deviation does not exceed one-twelfth of the normal population range. The 'normal' range is a composite of true differences between individuals and of differences introduced by the technical method (EGG). If the standard deviation of the method is one-twelfth of the population range it will cause the apparent range to be 5.4% larger than the true range (11).

In the 12 subjects of control group A for each item, gastric frequency, GFSD, and PR the standard deviation was calculated for the 4 separate recording sessions. To evaluate the reliability of EGG the mean of these 12 standard deviations was then compared with one-twelfth of the range found in the control group B of 52 subjects.

4.5.4 Results

Accuracy. In this part of the study a total of 14 hours of recording, divided into 42 periods of 20 min, were analysed. One recording session of 2 hours was performed on each postoperative day with two extra recordings of 2 hours on both day 3 after intravenous injection of glucagon and on day 4 when secretin was given.

The mean gastric ECA frequency, computed over the 20 min periods, in the serosal recordings varied between 0.026 and 0.058 Hz with a median of 0.050 Hz. Relatively low gastric ECA frequencies were observed especially during the first 2 postoperative days. No tachy-arrhythmias or tachygastrias, as typified by ECA frequencies 2-4 times higher than normal, were observed, either spontaneously or after glucagon or secretin had been given. The dysrhythmias observed were limited to frequency variations around the normal gastric ECA frequency at about 0.05 Hz, as is illustrated in fig. 4.5.2 and 4.5.3. This type of frequency variation was observed spontaneously in the first 3 postoperative days and also after glucagon and secretin had been given. In the serosal recordings no myoelectrical correlates of interdigestive migrating complexes were observed during the recording sessions.

When the mean gastric frequencies of corresponding periods of serosal and cutaneous time signals were compared, an identical frequency value was found in 22 of the 42 periods analysed.

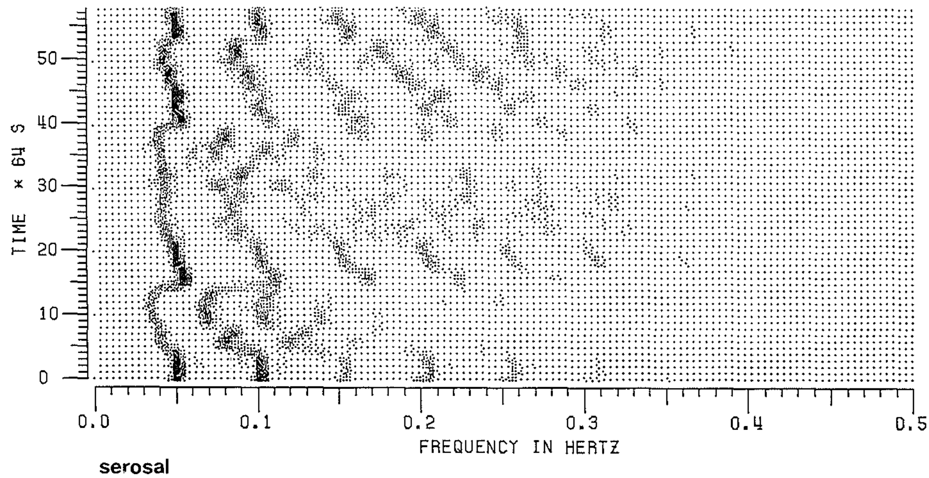


fig. 4.5.2 Grey-scale plot of a bipolar serosal signal after the i.v. administration of 0.5 mg glucagon showing the gastric ECA frequency at about 0.05 Hz and the multiple higher harmonics. The higher harmonics, a direct consequence of the waveform and the signal analysis technique, can be recognised in the spectrum because their frequency spacing forms exactly an integer.

An algebraic difference of 0.001 Hz was found in 14 of the periods analysed while in the remaining 6 periods a difference of 0.002 Hz was found.

The GFSD of the mean gastric ECA frequency (over the 20 min periods) in the serosal recordings, an indication for the stability, varied between 0.0022 and 0.0080 with a median of 0.0034. The difference between the GFSD in serosal and cutaneous recordings ranged from 0.0000 to 0.0006 with a median of 0.0002. There was no indication that the difference between serosal and cutaneous GFSD was any larger when the GFSD was higher.

In addition to the arithmetical comparison of the data, the grey-scale plots of the 20 min periods were compared by visual inspection with special attention being paid to the frequency variations, whether spontaneous or drug induced. In 84 of the 95 frequency variations of at least 0.004 Hz which were observed in the grey-scale plots of the serosal time signals, an identical frequency pattern was present in the corresponding grey-scale plots of the cutaneous time signals (fig. 4.5.4 and 4.5.5). The remaining 11 frequency variations visible in the grey-scale plots of the serosal time signal could not be recognized in the grey-scale plots of the cutaneous time signal. These 11 false-negatives were due to motion artefacts in the cutaneous time signal.

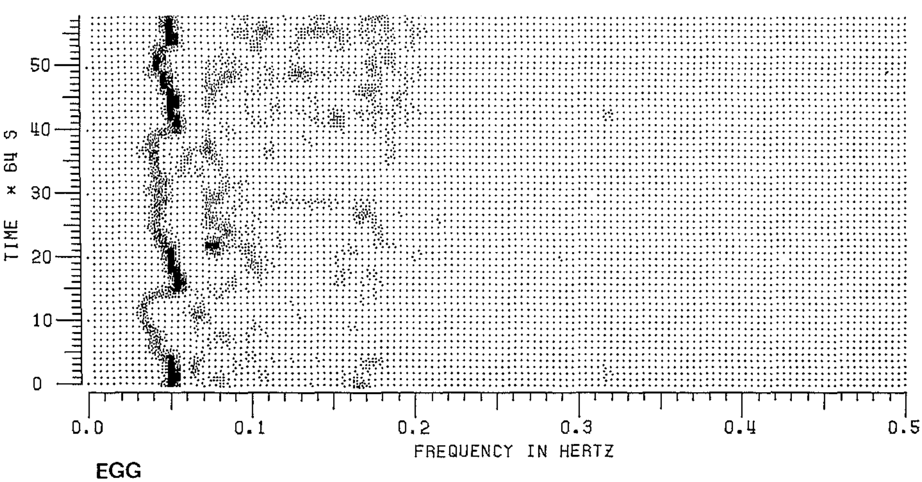


fig. 4.5.3 Grey-scale plot of the bipolar cutaneous signal, recorded simultaneously with the serosal signal shown in fig. 4.5.2. The plot clearly shows that the gastric frequency with the glucagon-induced dysrhythmias is identical to the dysrhythmias in the serosal recordings. Note the respiration signal between 0.15 and 0.20 Hz.

Reliability. The results in the control populations are summarized in table 4.5.1. In the 12 control subjects (group A) the EGG parameters (frequency, GFSD, and PR) fell within the range of the control population (group B). As can be seen from the comparison of columns 2 and 4 in table 4.5.1 EGG gives a reliable measure of gastric frequency and of its stability (expressed by the GFSD), but not of the PR.

Table 4.5.1.. Reliability; the range in a control population (group B) and one-twelfth of this range for comparison with the mean of the standard deviation of 4 separate recording sessions in 12 healthy subjects (group A).

	Control Group B n=52		Control Group A n=12	
Fasting state	median range	1/12 range	median range	stand. dev. of 4 EGGs*
Gastric ECA frequency (Hz)	0.050 0.045–0.055	0.0008	0.048 0.046–0.052	0.0007
GFSD	0.0028 0.0019–0.0040	0.00018	0.0025 0.0019–0.0034	0.00020
Postprandial state				
Gastric ECA frequency (Hz)	0.054 0.047–0.064	0.0014	0.051 0.049–0.057	0.0005
GFSD	0.0029 0.0019–0.0038	0.00016	0.0030 0.0024–0.0032	0.00017
Power ratio	6.79 2.08–16.61	1.21	6.32 2.64–11.71	1.56

* For each item the mean (of 12 observations) is given of the standard deviation of the 4 separate recording sessions in the 12 subjects.

4.5.5 Discussion

To evaluate the accuracy of EGG we decided to use implanted serosal electrodes in preference to intraluminal electrodes despite the invasive nature of the former, because the quality of the intraluminal signals is rather poor. Recordings with intraluminal electrodes are unsatisfactory because they do not permit the recognition of individual gastric ECA's.

This study confirms that the fundamental frequency in the electrogastrogram in man, called the gastric frequency, is of gastric origin and is equal to the repetition frequency of the gastric ECA. The small differences found fall within the resolution of the signal analysis method. Furthermore this study shows that EGG in combination with running spectrum analysis enables the recognition of small variations (0.004 Hz) in gastric ECA frequency. The only proviso is that there are no large motion artefacts in the electrogastrogram. It should be emphasized that, in contrast with visual interpretation (12), contamination of the electrogastrogram by frequencies of respiratory origin does not present a problem if running spectrum analysis is used.

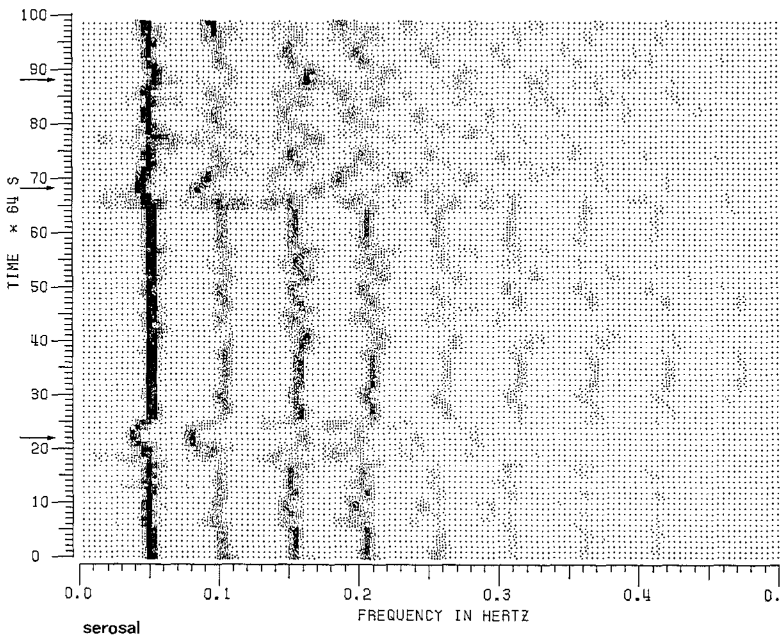


fig. 4.5.4 Grey-scale plot of a bipolar serosal signal showing the gastric ECA frequency at about 0.05 Hz and the multiple higher harmonics.

It was surprising that the electrical correlate of the interdigestive migrating complex (second components and/or spike activity) could not be discerned properly. This was probably due to the electrical properties of the electrodes (stainless steel) used in this study (13). Because of this we were not able to confirm previous findings (3,8,9) that ERA, the electrical correlate of motor activity, is reflected in the electrogastrogram by an amplitude increase.

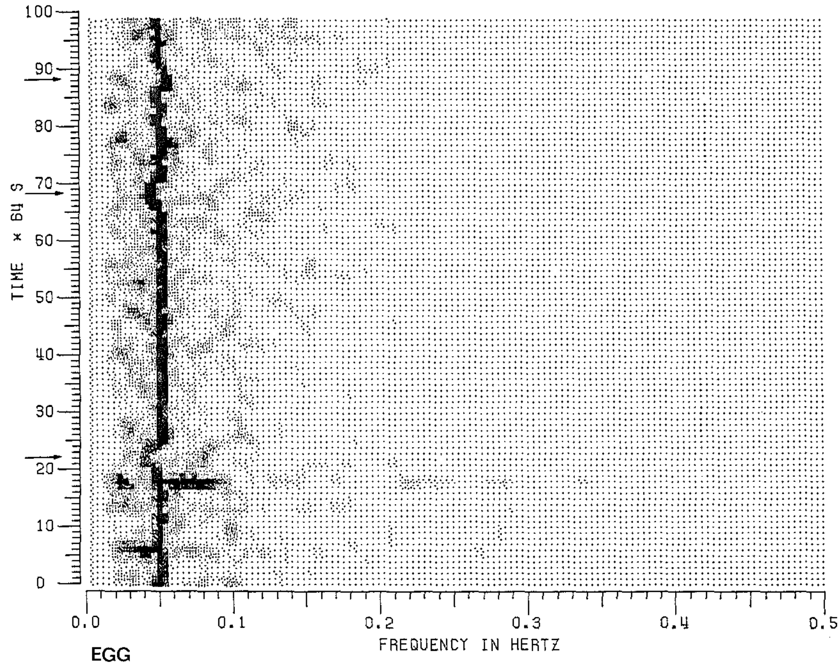


fig. 4.5.5 Grey-scale plot of the bipolar cutaneous signal, recorded simultaneously with the serosal signal shown in fig. 4.5.4. The plot clearly shows the gastric frequency variations identical to the variations in the serosal recordings. Note the motion artefact at about 17x64 seconds.

Although EGG in the present form gives an acceptable level of reliability for the gastric frequency and its stability (GFSD) it is not satisfactory for measuring the PR. Both the less reliable measurement of the PR and the large range for the PR in the control population (group B) can be explained by interdigestive motor activity and thus different power levels in the interdigestive state. We recently demonstrated that the power during phase II motor activity was a factor 2.61 (median, range 2.06-5.20) larger than during motor quiescence (phase I) (9). Because the duration of the recording in the fasting state is relatively short (30 min) with respect to the duration of one interdigestive cycle (125 ± 22 min) (14), the influence of the different power levels in the interdigestive state will be considerable and is responsible for the intra-individual variation in PR measured with EGG in the present form. Although these problems with the intra- and interindividual variation could be eliminated by lengthening the recording in the fasting state there is at present no indication that this is necessary in practice. In patients with chronic nausea and vomiting and with a delayed gastric emptying of solids a PR < 2.00 was found, which is clearly different from that for the control group (PR > 2.00) (15). This clear destinction is fortunate because it is our experience that if the recording period is lengthened the quality of the electrogastrogram is reduced because of an increase in the number of motion artefacts increases in the second part of the recording.

In a previous study (9) we observed a difference in gastric frequency and GFSD between motor quiescence (phase I) and phase II and III motor activity. Lengthening of the recording would probably enhance the reliability of EGG for these two parameters.

In conclusion, it can be said that the fundamental frequency in the electrogastrogram in man is of gastric origin and is equal to the repetition frequency of the gastric ECA. Electrogastrography in combination with running spectrum analysis enables the recognition of gastric ECA frequency variations. Electrogastrography gives a reliable measuring of the gastric ECA frequency and its stability, although it should be realized that the reliability is positively correlated with the duration of the recording in the fasting state because of variation in myoelectrical behaviour in the interdigestive state. Electrogastrography gives a less reliable measurement of the postprandial power increase, an indication for postprandial motor activity. This is due to the motor activity of the interdigestive migrating complex resulting in variable power levels in the fasting state. Lengthening of the fasting recording time would improve the reliability but at present it does not seem to be necessary for clinical application.

4.5.6 References

1. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transsection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.
2. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
3. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. What is measured in electrogastrography? Dig. Dis. Sci. 1980; 25: 179-187.
4. Nelson T.S., Kohatsu S. Clinical electrogastrography and its relation to gastric surgery. Am. J. Surg. 1968; 116: 215-222.
5. Brown B.H., Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.
6. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals recorded from dogs and man. In: Wienbeck M., ed. Motility of the digestive tract. New York: Raven Press, 1982: 241-250.
7. Blackman R.B., Tuckey J.W. The measurement of power spectra. Dover Publications Inc. New York, 1958.
8. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.
9. Geldof H., Van der Schee E.J., Grashuis J.L. Electrogastrographic characteristics of the interdigestive migrating complex in man. Am. J. Physiol. 1986; 250: G165-G171.
10. O'Brien P.C., Shampo M.A. Statistics for clinicians. Mayo Clin. Proc. 1981; 56: 573-575.
11. Barnett R.N. Medical significance of laboratory results. Am. J. Clin. Pathol. 1968; 50: 671-676.
12. Abell T., Tucker R., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in healthy humans shown by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.
13. Geddes L.A. Electrodes and the measurement of bioelectrical

events. Wiley Interscience, New York 1972.

14. Nishioka T., Sekuguchi T., Kogure M., Kusano M., Arai H., Katoh R., Okamura S., Matsuzaki T., Fukazawa T., Akiyama T., Ohwada H., Kobayashi S. A study on continuous simultaneous recordings of gastrointestinal motility and intraluminal PH in human healthy subjects. Jap. J. Gastroenterol. 1981; 78: 2065-2073.

15. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. An electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting. Gut 1986; 27: 799-808.

5. Electrogastrography in healthy subjects

5.1 Introduction

The results of EGG studies on gastric myoelectrical activity in healthy subjects are reported in this chapter. The electrogastrographic characteristics of the gastric myoelectrical behaviour in the interdigestive state are described in section 5.2. The possibility of using these characteristics to detect the different phases of the interdigestive migrating complex by EGG is evaluated. In section 5.3 normal ranges for several EGG parameters in a control population are defined. In section 5.4 a preliminary attempt is made to analyse the control mechanism of the postprandial frequency and power pattern.

5.2. ELECTROGASTROGRAPHIC CHARACTERISTICS OF THE INTERDIGESTIVE MIGRATING COMPLEX IN MAN

Published in American J. of Physiology 1986; 250: G165-G171.
Co-authors E.J. van der Schee, J.L. Grashuis.

5.2.1 Abstract

Interdigestive myoelectrical activity and mechanical activity were studied simultaneously by means of cutaneous electrodes (electrogastrography) and intraluminal pressure recording, respectively, in 10 healthy male volunteers. The aims of the present study were: 1) to describe the characteristics of the electrogastrogram during the different phases of the interdigestive migrating complex (IMC) in healthy subjects, and 2) to determine to what extent these characteristics can be used to identify the different phases of the IMC. The electrogastrograms were analysed visually and by running spectrum analysis. It was concluded that in man the gastric frequency present in the electrogastrogram appears to be less stable during motor activity than during motor quiescence, in particular during phase III, but far more stable than its canine counterpart. A small but consistent drop in gastric frequency was observed at the change-over from motor quiescence to phase II motor activity. The power of the gastric frequency increased with increasing motor activity, except during phase III. A characteristic frequency and power behaviour during phase III could only be recognized in a minority of the IMCs. In general electrogastrography cannot, given the present state of the art, be used to precisely identify the different phases of the IMC.

5.2.2 Introduction

The activity front of the interdigestive migrating complex (IMC) is an important marker of several physiological events in the gastrointestinal tract (9,16,30). Non-invasive detection of the different phases of the IMC, according to the classification of Code and Marlett (6), would be a welcome aid in the study of interdigestive motor and secretory activity. As the control mechanism of intestinal motility is of an electrical nature, electrogastrography (EGG), the recording of gastric myoelectrical activity by means of cutaneous electrodes, might make this possible.

The stomach has an inherent rhythmic myoelectrical activity with a repetition frequency of about 0.05 Hz (3 cycles/min), which is referred to as electrical control activity (ECA) (14,22). When motor activity is present, the ECA (also known as basic electric rhythm or slow waves) is accompanied by a second component, with or without superimposed fast oscillating potential changes called spike potentials, in this study referred to as electrical response activity (ERA) (22).

The electrogastrographic signal can be considered as a summation of time-shifted waveforms generated by the ECA and, if present, the contraction-related ERA travelling along the stomach (25). It has been well established that the fundamental frequency of the electrogastrogram in both dog and man is of gastric origin and equals the repetition frequency of the ECA (1,5,13,25). Motor activity generally manifests itself in the electrogastrogram by an increase in amplitude of the gastric frequency (25,31). This phenomenon has been observed most consistently in the postprandial state (12,13,26).

Van der Schee and Grashuis (28) recently demonstrated that interdigestive contractile activity in the dog could be recognized in the running spectrum representations of electrogastrograms (based on fast Fourier transformation) by the appearance of high-power low-frequency components, with frequencies between 0.085 Hz (the normal gastric frequency in dogs) and about 0.01 Hz. The gastric myoelectrical characteristics of the fasting contractile activity in humans have never been described. Manometrical studies, however, indicate that the interdigestive motor pattern in man is different from that found in dogs. Whereas during phase III in dogs groups of strong contractions alternate with short periods (0.5 - 1 min) of motor quiesence or very weak contractions (10,15,21), in humans gastric phase III activity (lasting for about 4 - 6 min.) seems to be more regular while phase IV is very short or missing altogether (8,17). Moreover not all activity fronts appear to originate in the stomach. Instead the duodenum is found to be the point of origin (11,20).

The objectives of the present study were twofold: 1) to describe the electrogastrographic characteristics during the different phases of the IMC in humans, and 2) to determine to what extent these characteristics can be used to identify the phases of the IMC.

5.2.3 Materials and methods

Subjects. Ten healthy male voluteers (median age 25 year, range 19 - 40) were studied. After an overnight fast, both intraluminal pressure and electrogastrographic recordings were made during a period of approximately 3 hours.

Recording of motor activity in the stomach and duodenum. In 4 subjects intraluminal pressure recordings were made using three semiconductor strain-gauge pressure transducers mounted 5 cm apart in a commercially available pressure probe (model 31, Kulite semiconductor products, Inc., New Jersey). In 6 subjects the pressure activity was recorded by a low compliance perfusion system originally described by Arndorfer et al (3). The distances between the 3 recording sites were 5 cm (proximally) and 7 cm (distally). The tubes were perfused with distilled water via a pneumohydraulic pump (perfusion rate 0.6 ml/min). Intraluminal pressure changes were recorded continuously using strain gauge transducers attached to each tube.

Both probes contained radiopaque markers at each recording site enabling careful positioning under fluoroscopic control. Two recording sites were positioned in the antrum and 1 in the duodenum. All signals were recorded on a paper chart (Van Gogh

EP-8b) and simultaneously stored on magnetic tape (Racal Store 14). The motor activity of phase II was quantified by summing the amplitude force (kPa) of the recorded pressure waves during a 10 min period preceding phase III.

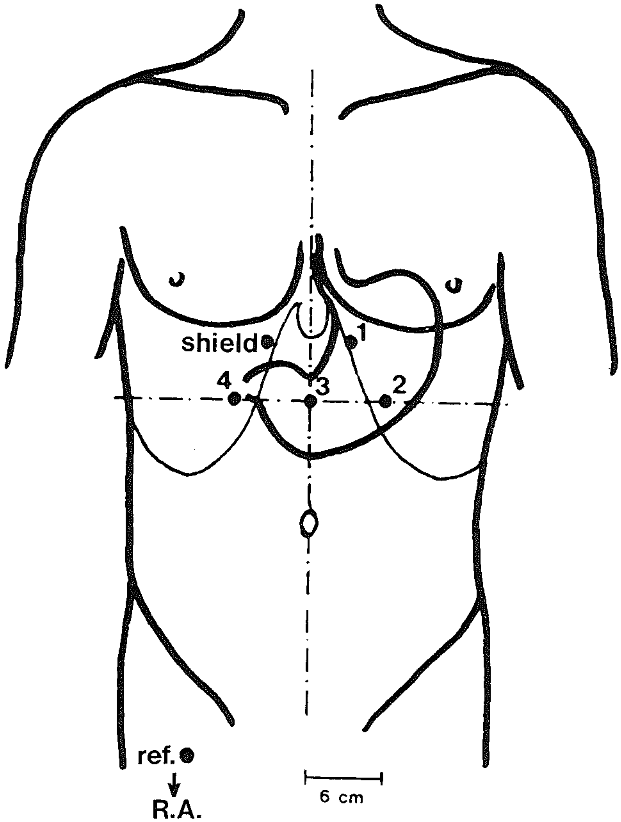


fig. 5.2.1 Electrode positions used in this study. Electrodes 2,3 and 4 are situated on a transverse line halfway between lower end of sternum and umbilicus. Electrode 3 is placed at intersection of this line and median plane. Distance between all abdominal electrodes is 6 cm. Reference electrode is placed on right ankle. The shield electrode is used to reduce possible interference from 50 Hz mains voltage at input stage of preamplifiers.

Recording of gastric myoelectrical activity. In most subjects the electrogastrogram bipolarly recorded from two electrodes placed along the antral axis is of good quality (13,19). However, standard electrode positions cannot be defined precisely because of interindividual anatomical variations (12,26). Therefore several leads were used and the lead with the best signal-to-noise ratio was then selected for further analysis. The positions of the 6 recessed-type electrodes (Red Dot 2256, 3M Co.) are shown in fig. 5.2.1. A strain-gauge respiration transducer was attached to the thoracic wall.The 4 monopolar, the 6 bipolar signals and the respiration signal were recorded on a paper chart (Van Gogh EP-8b) and simultaneously stored on magnetic tape (Racal Store 14). The high and low pass filters (6 decibel/octave) were set at 0.012 and 0.46 Hz respectively.

Signal analysis. The electrogastrogram contains frequency, amplitude and waveform information. Tracings were analysed by visual inspection and by running spectrum analysis, a computerized frequency or spectral analysis. We limited visual inspection of the electrogastrogram in this study to amplitude changes. In running spectrum analysis, using a fast Fourier transform, power spectra of short overlapping stretches of a time signal (in this study the electrogastrogram) are computed and displayed as a function of time, thus yielding frequency and amplitude information over the course of time (27). No waveform analysis has been performed.

A fast Fourier transform algorithm implemented on a NOVA 2 digital computer was used to obtain the power spectra of the time signals. These signals, replayed from tape 16 times faster than real time, were preprocessed by band-pass filtering using a Butterworth filter (24 decibel/octave) with (real time) cut-off frequencies set at 0.01 and 0.5 Hz, to remove possible DC components and to avoid aliasing. They were then digitized (real time sampling frequency 1 Hz) and fed into the computer. Spectra were obtained as follows: every 64 s a power spectrum was computed from the preceding 256 s of the EGG time signal, to which a Hamming window was applied to reduce leakage (4). These time values have been shown to be satisfactory for the extraction of relevant information from the electrogastrogram, giving 129 points per spectrum and a frequency spacing of 0.0039 Hz (27). This procedure generates series of spectra that overlap in time, called running spectra, which we plotted in two different ways: pseudo-3-dimensional and grey-scale plots. The grey-scale plot enables the easy recognition of frequency changes in course of time. Power and thus amplitude changes (the amplitude is the square root of the power) can be recognized more precisely in the pseudo-3-dimensional plot. Plots were made on a Versatec 1100 A printer plotter. During processing each computed spectrum was drawn, together with its spectrum number, on a Tektronix 4010 display terminal with hard copy facilities. Where there were problems of interpretation after completion of the processing each spectrum could be analysed in detail. The mean gastric frequency (Hz), with standard deviation (SD), and its power content were computed for the several phases of the IMC in the stomach as they were identified by pressure recordings. The SD was used as a measure for the stability of the gastric frequency. The larger the SD the more unstable is the gastric frequency in the period analysed. When the activity front did not originate in the stomach, the duodenal IMC phases were used to determine which signal stretches had to be analysed.

Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance to the stomach wall) it is impossible to make a comparison of inter-individual power data. Therefore only power changes within each separate recording session were used for statistical analysis.

The study was approved by the Medical Ethics committee of the Erasmus University, Rotterdam, on June 4, 1982 and carried out with the written informed consent of the subjects.

Statistical analysis. The Wilcoxon signed-rank-test was used to evaluate if a significant difference existed between the different phases of the IMC in mean gastric frequency, standard deviation (SD) and its power content (2,23). To calculate the coefficient of correlation (r) between the gastric motor activity and the power of the gastric frequency, the Spearman rank correlation test was used (23). Probability (p) values were derived from two tailed tests. The level of significance used in this study was 0.05.

5.2.4 Results

From the 21 IMC activity fronts recorded with intraluminal pressure recordings in the 10 volunteers, 16 originated in the stomach and the other 5 originated in the duodenum. The median duration of gastric phase III was 4 min (range 3 - 6).

Characteristics of the 16 IMCs originating in the stomach.

Visual inspection. Motor quiescence (phase I) was characterized by a constant low amplitude electrogastrogram.

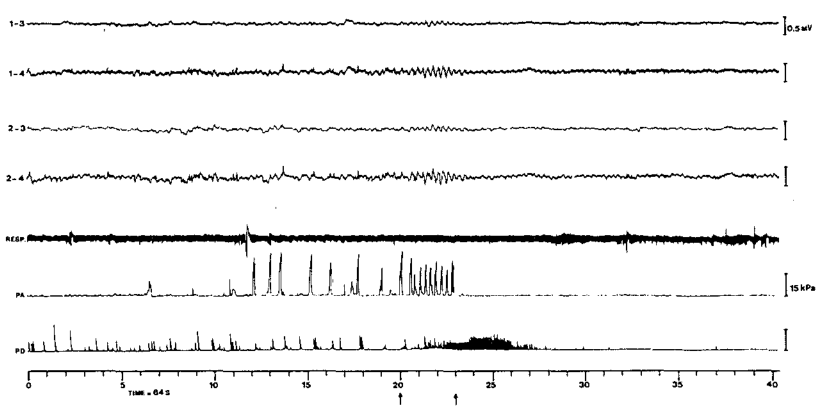


fig. 5.2.2 Four bipolar time signals, respiration signal, mechanical activity in antrum (Pa), duodenum (Pd) and time scale. During phase III, marked with ->, an amplitude increase can be recognized followed by a decrease at the change-over to motor quiescence.

At the change-over from motor quiescence to motor activity (phase II) a gradual increase in amplitude could be distinguished in 10 IMCs. In 3 IMCs this amplitude increase occurred some time (5-10 min) before motor activity was recorded. At the change-over to phase III an obvious amplitude increase was seen in 6 IMCs as illustrated in fig. 5.2.2, while in the remaining 6 IMCs phase III appeared to be indistinguishable from phase II (see fig. 5.2.3).

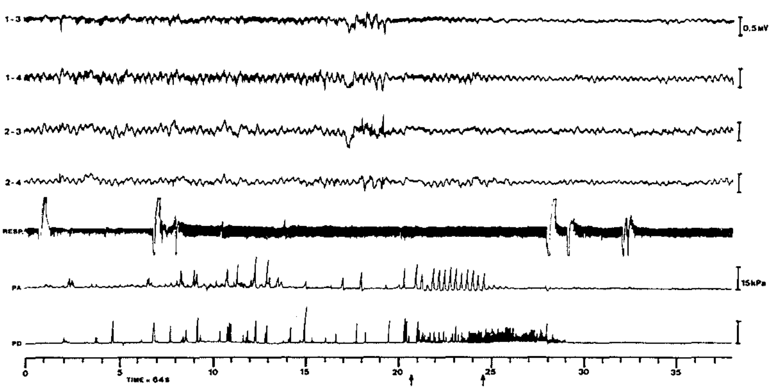


fig. 5.2.3 Four bipolar time signals, respiration signal, mechanical activity in antrum (Pa), duodenum (Pd) and time scale. Phase III, marked with ->, cannot be recognized in the electrogastrogram. Leaving the part of electrogastrogram during phase III out of consideration an amplitude difference can be seen between phase II and phase I.

At the change-over from motor activity to motor quiescence (phase I) an amplitude decrease could only be recognized with certainty in 12 IMCs (fig. 5.2.2 and 5.2.3). No amplitude changes could be recognized in 4 IMCs predominantly because of the respiration artefact present in the electrogastrogram.

Running spectrum analysis. Mean gastric frequency, its standard deviation (SD) and power changes in the different IMC phases, expressed as median and range, are summarized in table 5.2.1.

Table 5.2.1. Comparison of findings during different phases of IMC originating in stomach and duodenum.

IMC	Phase I	Phase II	Phase III
	Stomach (n = 16)		
Gastric	0.049	0.047	0.048
frequency (Hz)	0.043–0.052	0.041–0.052	0.041–0.056
SD	0.0019	0.0029	0.0042
	0.0014–0.0023	0.0021–0.0043	0.0024–0.0060
Power increase		2.61*	0.76†
		2.06–5.20	0.05–3.95
	Duodenum (n = 5)		
Gastric	0.050	0.050	0.050
frequency (Hz)	0.049–0.051	0.048–0.051	0.049–0.053
SD	0.0022	0.0024	0.0023
	0.0018–0.0026	0.0020–0.0029	0.0020–0.0026
Power increase		1.17*	0.81†
		1.02–2.18	0.46–1.04

Values represent medians and ranges; n, no. * Power increase at the changeover from phases I to II. † Power increase at the changeover from phases II to III.

Phase I was characterized by a very stable gastric frequency as is shown by the low value of the frequency SD. The initial power of the gastric frequency in phase I was relatively low. In 6 IMCs the power started to increase 5 - 10 minutes before phase II motor activity was evident in the pressure recordings. In the other 10 IMCs the power increase was synchronous with the start of phase II motor activity. Because of this early power increase only the first 10 minutes of the electrogastrogram corresponding to phase I following the motor activity front were used for computing the mean gastric frequency, SD and power of this phase.

In all 16 IMCs the gastric frequency during phase II appeared to be less stable ($p<0.01$) and lower ($p<0.01$) than during phase I. The power of the gastric frequency in phase II was, at least a factor 2, larger than in the first 10 min of motor quiescence following phase III ($p<0.01$). This increase in power was positively correlated with the motor activity recorded during a 10 min long period of phase II preceding phase III ($r = 0.96$; $p < 0.0001$).

The characteristics of phase III varied considerably both with respect to the frequency and the power behaviour. A clear, identical frequency and power behaviour was found in only 7 IMCs, which could easily be recognized in the pseudo-3-dimensional and grey-scale plot as illustrated in fig. 5.2.4 and 5.2.5.

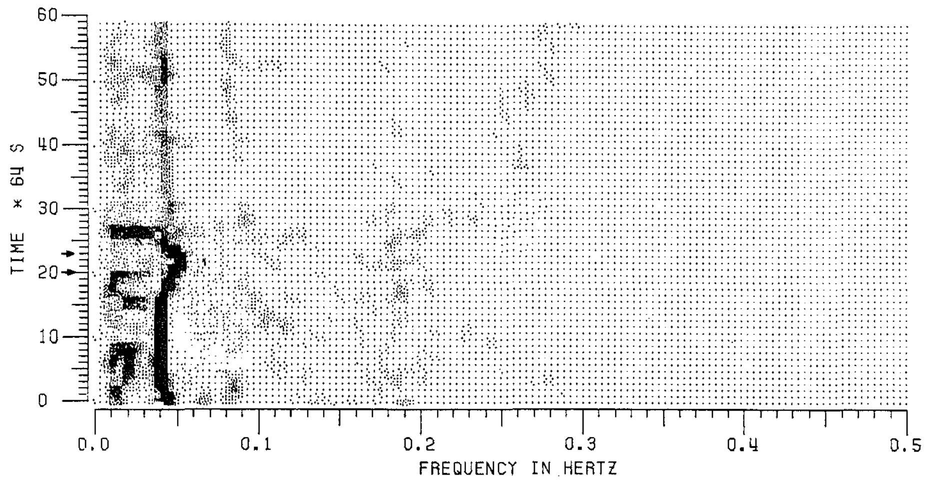


fig. 5.2.4 Grey-scale plot of the electrogastrogram shown in fig. 5.2.2 (lead 2-4). Note characteristic frequency behaviour during phase III of this IMC marked with ->. Low-frequency components at about 0.01 - 0.03 Hz can be seen throughout the analysed period, although they tend to be less powerful during motor quiescence.

During phase III of these 7 IMCs a power increase and a relatively stable, somewhat increased gastric frequency were observed, followed by a decrease in frequency and power. In the other 9 IMCs no specific frequency and power behaviour could be discerned. The gastric frequency during phase III in the majority of the IMCs was found to be relatively unstable ($p<0.01$) as shown by the large frequency SD. The power behaviour also varied, and a power increase, no power change or even a power decrease was observed with respect to the power level of phase II (fig. 5.2.6).

Low-frequency components (0.01-0.03) were observed in all subjects (fig. 5.2.4 and 5.2.6), but no correlation between these low-frequency components and motor activity existed.

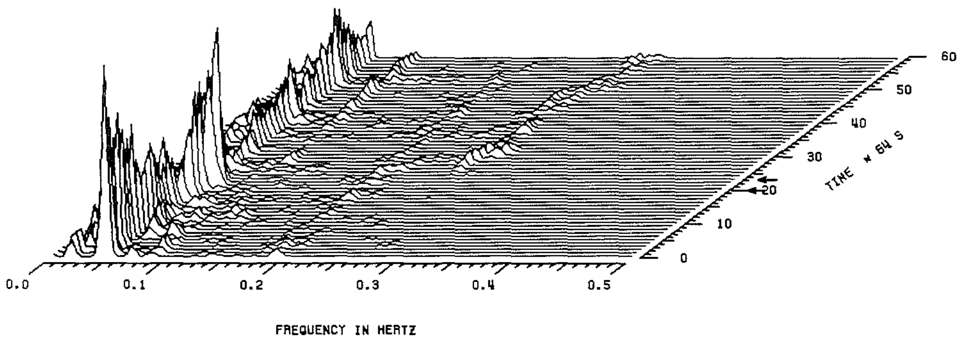


fig. 5.2.5 Pseudo-3-D display of the electrogastrogram shown in fig. 5.2.2 (lead 2-4). The power changes at the change-over from phase II to phase III and subsequently to motor quiescence can be easily recognized. The frequency at about 0.1 Hz is the second harmonic. The frequency at about 0.2 - 0.3 Hz is of respiratory origin. Phase III marked with ->.

Characteristics of the 5 IMCs originating in the duodenum.

Visual inspection. The electrogastrogram showed an amplitude decrease following a marked phase-II-like motor activity in the stomach in only 1 IMC cycle. In the other 4 IMCs no or weak motor activity was observed in the stomach with intraluminal pressure recording. The electrogastrograms recorded during these 4 IMCs showed no recognizable amplitude alterations.

Running spectrum analysis. The results of the running spectrum analysis are summarized in table 5.2.1. No changes in the gastric frequency were observed. With the change-over from motor quiescence to motor activity a power increase (factor 2.18) was found in 1 IMC coinciding with the phase-II-like motor activity in the stomach. The power changes observed in the remaining IMCs originating in the duodenum were smaller, corresponding to the less marked phase-II-like motor activity or absent motor activity in the stomach.

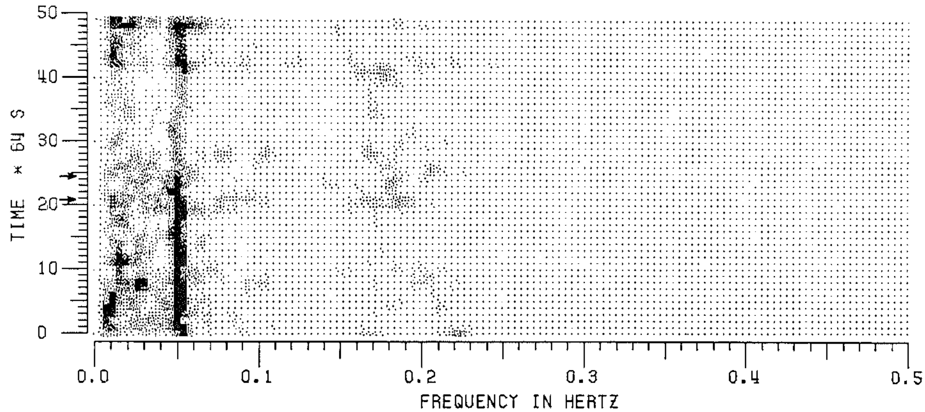


fig. 5.2.6 Grey-scale plot of the electrogastrogram shown in fig. 5.2.3 (lead 2-4). During phase III, marked with ->, no frequency changes can be seen. Only the power decrease at the change-over from motor activity to motor quiescence (phase I) can be recognized. At the change-over from phase II to phase III a small power decrease (0.90) was present, which cannot be recognized in the grey-scale plot. Low-frequency components at about 0.01 - 0.03 Hz can be seen throughout the analyzed period. The power increase at line 42 coincides with the start of phase II motor activity.

5.2.5 Discussion

Our findings with regard to the characteristics of the IMCs as measured with intraluminal pressure recording techniques are in agreement with those reported in the literature (7,11,18,20,29).

Considering the closely related physiological functions of the GI-tract, the detection of the different phases of the IMC using a non-invasive method would in theory be an interesting application of EGG. Our study has shown that visual inspection of the electrogastrogram cannot be reliably used to identify IMC phases. Amplitude changes can only be interpreted as such from good quality electrogastrograms, i.e. those devoid of respiration artefacts.

Running spectrum analysis lends itself to a better and quantitative approach. The characteristic frequency (and power) behaviour during phase III as is shown in fig. 5.2.4 and 5.2.5 can be considered to be indicative of this phase but was only observed in a minority (44%) of the IMCs. During phase II the power was at least a factor 2 larger than during the initial 10 minutes of phase I. This difference in power, observed in all 16 IMCs, can be easily seen in grey-scale plots or pseudo-3-D plots, and can be used, in combination with the very stable gastric frequency in the initial period of phase I, to estimate the end of motor activity and the beginning of phase I. However the variable power of the gastric frequency during phase III prevents an exact timing of this change-over. In addition the change-over from phase I to phase II cannot be exactly determined with EGG. Whatever the cause of the gradual power increase at the change-over from phase I to phase II, before motor activity is recorded, this phenomenon prevents the identification of the exact boundary between phases I and II.

With regard to the low-frequency components it is worthwile comparing the electrogastrographic characteristics of the IMC in humans with those in dogs as described by Van der Schee and Grashuis (28). These authors showed that in fasting dogs the presence in the electrogastrogram of high power low-frequency components and absence of the normal gastric frequency (0.085 Hz in dogs) were indicative of phase III motor activity. They also showed that the mechanism through which this is brought about involves highly variable, prolonged, ECA interval durations associated with phase III contractions (24). In man this type of low-frequency components were not observed. Instead a relatively stable gastric frequency was found in all human IMCs. These observations suggest that in man during phase III such variability in ECA interval duration does not occur. We conclude therefore that in man the gastric ECA frequency during the motor activity front of the IMC is far more stable than its canine counterpart.

In general the power of the gastric frequency in the electrogastrogram increases when motor activity is present (13,25,31). This is in agreement with the finding that the power of the gastric frequency found during periods of phase II motor activity was higher than during periods of motor quiescence. However, two questions of considerable interest arise. 1) Why did the power start to increase in phase I before motor activity was seen in the pressure recordings? Does the technique of pressure recording fail to record weak motor activity? Intraluminal pressure recording in the stomach could be unsatisfactory due to the non-tubular anatomy of the stomach (32). 2) Why was an increase in power during phase III not observed in all IMCs? This unexpected behaviour, which is in contrast with phase II where a significant positive correlation was present between power increase and motor activity, cannot be explained with our present state of knowledge.

Referring back to the objectives of our study we can now summarize: 1) The gastric frequency appeared to be less stable during motor activity, in particular during phase III, than during motor quiescence, but far more stable than its canine counterpart. 2) A small but consistent drop in gastric frequency could be observed at the change-over from motor quiescence to phase II motor activity. 3) The power of the gastric frequency increased with increasing motor activity, except during phase III. 4) A characteristic frequency and power behaviour during phase III could only be recognized in a minority of the IMCs.

We conclude that, given the present state of the art, neither visual inspection nor running spectrum analysis can be used to exactly identify the different phases of the IMC.

5.2.6 References

1. Abell T.L., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in humans shown by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.
2. Armitage P. Statistical Methods in Medical Research. New York, Wiley, 1971: 396.
3. Arndorfer R.C., Steff J.J, Dodds W.J., Lineham H.J., Hogan W.J. Improved infusion system for intraluminal esophagal manometry. Gastroenterology 1977; 73: 23-27.
4. Blackman R.B., Tuckey J.W. The Measurement of Power Spectra. New York, Dover Publications Inc. 1958.
5. Brown B.H., Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.
6. Code C.F., Marlett J.A. The interdigestive myo-electric complex of the stomach and small bowel of dogs. J. Physiol. (London) 1975; 246: 289-309.
7. Daniel E.E., Fox J.E.T., Collins S.M., Lewis D., Meghji M., Track N.S. Initiation of migrating myoelectric complexes in human subjects: role of duodenal acidification and plasma motilin. Can. J. Pharmacol. 1981; 59: 173-179.
8. Defilippi C., Valenzuela J.E. Sham feeding disrupts the interdigestive motility complex in man. Scan. J. Gastroenterol. 1981; 16: 977-979.
9. Dent J., Dodds W.J., Hogan W.J., Sekuguchi T. Interdigestive phasic contractions of the lower esophagal sphincter (LES) in humans. Clinical Research 1978; 26: 705.
10. Ehrlein H.J. A new technique for simultaneous radiography and recording of gastrointestinal motility in unanesthetized dogs. Lab. Anim. Sci. 1980; 30: 879-884.
11. Finch P., Ingram D., Henstridge J., Catchpole B. The relationship of sleep stage to the migrating gastrointestinal complex of man. In: Gastrointestinal Motility, edited by Christensen J. New York: Raven Press, 1980: 261-265.
12. Geldof H., Van der Schee E.J., Smout A.J.P.M., Grashuis J.L.

Electrogastrography. In: Gastric and Gastroduodenal Motility, edited by Akkermans L.M.A., Johnson A.G., Read N.W. New York: Praeger, 1984: 163-174.

13. Hamilton J.W., Bellahsene B., Reichelderfer M., Webster J.G., Bass P. Simultaneous mucosal and surface recording of the human electrogastrogram. In: Electrogastrography; methodology, validation, and application, edited by Stern R.M., Koch K.L. New York, Praeger Publishers, 1985: 132-142.

14. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transsection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.

15. Itoh Z., Aizawa I., Takeuchi S., Takayanagi R. Diurnal changes in gastric motor activity in conscious dogs. Am. J. Dig. Dis. 22: 1977; 117-124.

16. Itoh Z., Takahashi I. Periodic contractions of the canine gallbladder during the interdigestive state. Am. J. Physiol. 1981; 240: G184-G189.

17. Itoh Z., Sekiguchi T. Interdigestive motor activity in health and disease. Scan. J. Gastroenterol. 1982; 18(suppl.82): 121-134.

18. Lux G., Lederer P., Femppel J., Rosch W., Domschke W. Spontaneous and 13-NLE-Motilin induced interdigestive motor activity of esophagus, stomach and small intestine in man. In: Gastrointestinal Motility, edited by Christensen J. New York: Raven Press, 1980: 269-277.

19. Mirizzi N., Scafoglieri U. Optimal directions of the electrogastrographic signal in man. Med. Biol. Eng. Comp. 1983; 21: 385-389.

20. Nishioka T., Sekiguchi T., Kogure M., Kusano M., Arai H., Katoh R., Okamura S., Matsuzaki T., Fukazawa T., Akiyama T., Ohwada H., Kobayashi S. A study on continuous simultaneous recordings of gastrointestinal motility and intraluminal pH in human healthy subjects. Jap. J. Gastroenterol. 1981; 78: 2065-2073.

21. Ormsbee H.S., III, Koehler Jr S.L., Telford G.L. Somatostatin inhibits motilin-induced interdigestive contractile activity in the dog. Am. J. Dig. Dis. 23: 781-788, 1978.

22. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
23. Siegel S. Nonparametric Statistics for the Behavioral Sciences. New York, McGraw-Hill, 1956: 75-83.
24. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. Gastric pacemaker rhythm in conscious dog. Am. J. Physiol. 1979; 237: E279-E283.
25. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. What is measured in electrogastrography? Dig. Dis. Sci. 1980; 25: 179-187.
26. Smout A.J.P.M., Van der Schee E.J., Akkermans L.M.A., Grashuis J.L. Recording of gastrointestinal activity from surface electrodes. Scan. J. Gastroenterol. 1984; 19(suppl.96): 11-18.
27. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals recorded from dogs and man. In: Motility of the Digestive Tract, edited by Wienbeck M. New York, Raven Press, 1982: 241-250.
28. Van der Schee E.J., Grashuis J.L. Contraction-related low-frequency components in canine electrogastrographic signals. Am. J. Physiol. 1983; 240: G470-G475.
29. Vantrappen G., Janssens J., Hellemans J., Ghoos Y. Interdigestive motor complex of normal subjects and patients with bacterial overgrowth of small intestine. J. Clin. Invest. 1977; 59: 1158-1166.
30. Vantrappen G.R., Peeters T.L., Janssens J. The secretory component of the interdigestive migrating motor complex in man. Scan. J. Gastroenterol. 1983; 14: 663-667.
31. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.
32. You C.H., Chey W.Y. Study of electromechanical activity of the stomach in humans and dogs with particular attention to tachygastria. Gastroenterology 1984; 86: 1460-1468.

5.3 GASTRIC MYOELECTRICAL BEHAVIOUR IN HEALTHY SUBJECTS STUDIED BY STANDARD ELECTROGASTROGRAPHY

5.3.1 Introduction

Before studying patient groups with EGG it was necessary to describe the gastric myoelectrical behaviour in a large control population. Normal ranges for the several EGG parameters discussed in section 4.3, had to be established. The influence of age and sex on the EGG parameters was also studied, as there is some evidence that the gastric frequency increases with age (53).

The objective of the present study was to characterize the fasting and postprandial myoelectrical activity in a control population and to define normal values for the several EGG parameters.

5.3.2 Materials and methods

Fifty-two healthy subjects, 27 men and 25 women (mean age 42, range 16-75 yrs.) participated in the study. None of them had a history of gastrointestinal or systemic disorders.

The study was approved by the Medical Ethics committee of the Erasmus University, Rotterdam, on June 4, 1982 and carried out with the informed consent of the subjects.

The recording techniques are described in the sections 4.2 and 4.4. The methods used for signal analysis and data presentation are identical to those described in section 4.3.

Statistical analysis. Regression lines (least square method) and coefficients of correlation (r) were calculated for normally distributed data, otherwise the Spearman rank correlation coefficient was calculated. Probability (p) values were derived from two-tailed tests with 0.05 as the significant level.

5.3.3 Results

The results in the control group are summarized in table 5.3.1.

Table 5.3.1. EGG parameters in the control population.

	Control group n=52			
	median	mean	stand.dev.	range
Fasting state				
Frequency (Hz)	0.050	0.050	0.0028	0.045–0.055
Standard deviations (SD)	0.0028	0.0028	0.00057	0.0019–0.0040
Instability factor (IF)	1.12	1.15	0.11	1.00–1.40
Second harmonics*	38.5%			
Postprandial state				
Frequency (Hz)	0.054	0.055	0.0046	0.047–0.064
Standard deviations (SD)	0.0029	0.0028	0.00051	0.0019–0.0038
Instability factor (IF)	1.10	1.12	0.10	1.00–1.40
Second harmonics*	67.3%			
Power ratio (PR)	6.79	7.48	4.45	2.08–16.61

The presence of second harmonics is expressed in %.

An example of an electrogastrogram is shown in fig. 5.3.1.

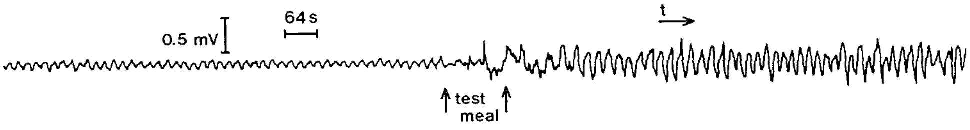


fig. 5.3.1 Electrogastrogram of a control subject. Note the postprandial amplitude increase.

The pseudo-3-dimensional and the grey-scale plot plot shown in fig. 5.3.2 and 5.3.3 were representative for this group. In the fasting state a gastric frequency of relatively low power was found with negligible frequency variations, as was indicated by a small standard deviation (SD) and an instability factor (IF) close to 1. These parameters confirmed the impression obtained by visual inspection of the grey-scale plots that the fasting frequency in healthy subjects is stable.

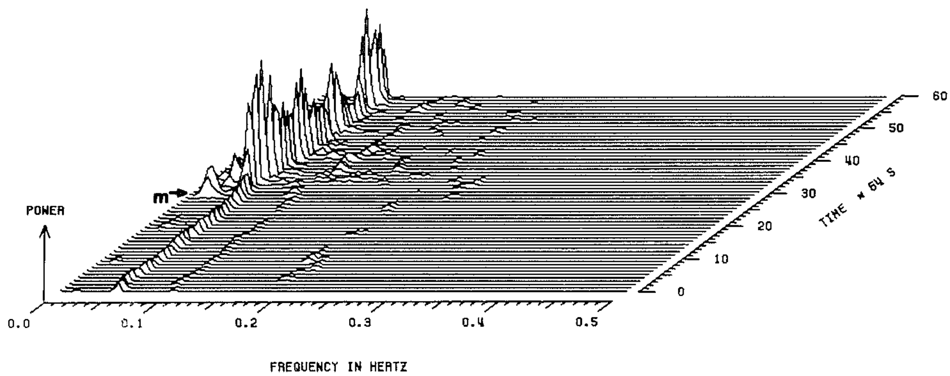


fig. 5.3.2 Pseudo-3-D display of the electrogastrogram shown in fig. 5.3.1. Note the postprandial power increase of the gastric ECA frequency at 0.050 Hz after the test meal marked with 'M'. A second harmonic is present both in fasting and postprandial state at 0.10 Hz.

Table 5.3.2. Frequency dip parameters in the control population.

		Control Group n=52			
		median	mean	stand. dev.	range
F_{max}	(Hz)	0.056	0.056	0.0045	0.047–0.064
F_{min}	(Hz)	0.037	0.038	0.0027	0.035–0.043
T_{max}	(min)	12	12.1	2.17	7–15
T_{min}	(min)	3	2.8	0.71	2–4
T_d	(min)	9	9.1	1.78	6–12
T_s	(min)	5	5.4	1.08	4–8

Immediately after the test meal a 'frequency dip' was seen in every subject. The characteristics of this frequency dip were quantitatively analysed, using the grey-scale plots and detailed analysis of the individual spectra obtained from the 52 subjects.

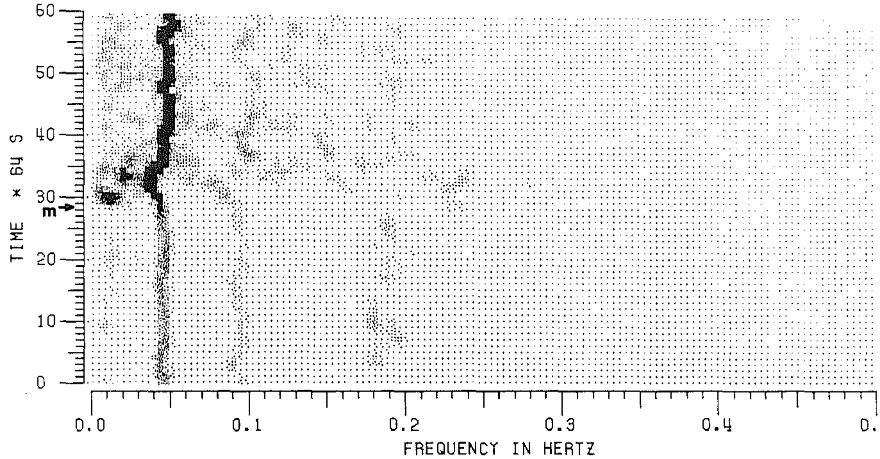


fig. 5.3.3 Grey-scale plot of the electrogastrogram shown in fig. 5.3.1. Note the frequency dip following the ingestion of the test meal marked with 'M'. Postprandial power increase is expressed by the increased blackness. Frequencies at about 0.20 Hz are of respiratory origin.

The parameters used to quantify the frequency dip are graphically presented in fig 5.3.4. The results are summarized in table 5.3.2. The average frequency decrease in these 52 subjects was 23% of the fasting frequency. After about 5 min. the frequency started to increase again and generally rose to a level equal to or temporarily higher than the fasting frequency.

After this frequency dip the gastric frequency, referred to as the postprandial frequency, stabilized at a level which was at least equal to or somewhat higher than during the fasting state. The range of the postprandial SD and IF was practically the same as in the fasting state, thereby confirming the impression obtained by visual inspection of the grey-scale plots that the postprandial frequency was also stable.

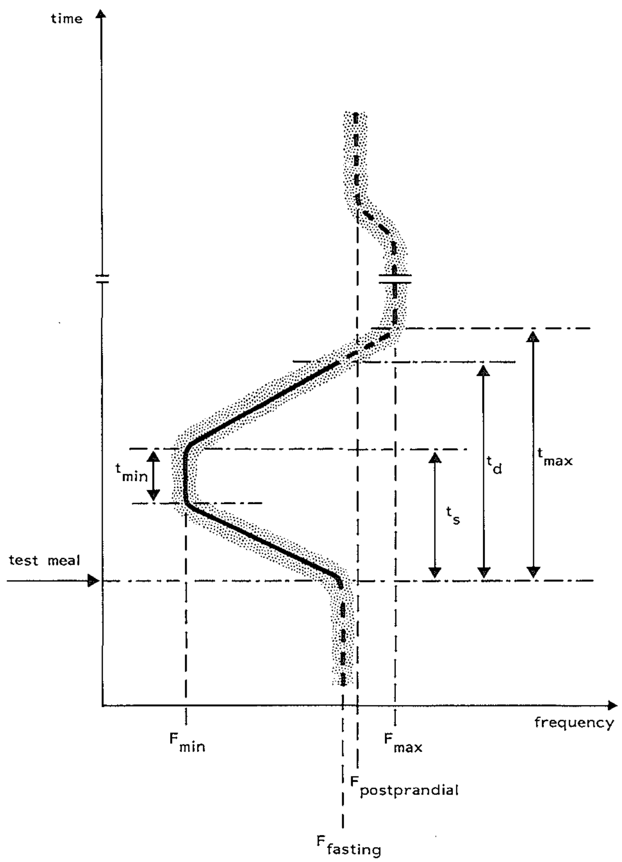
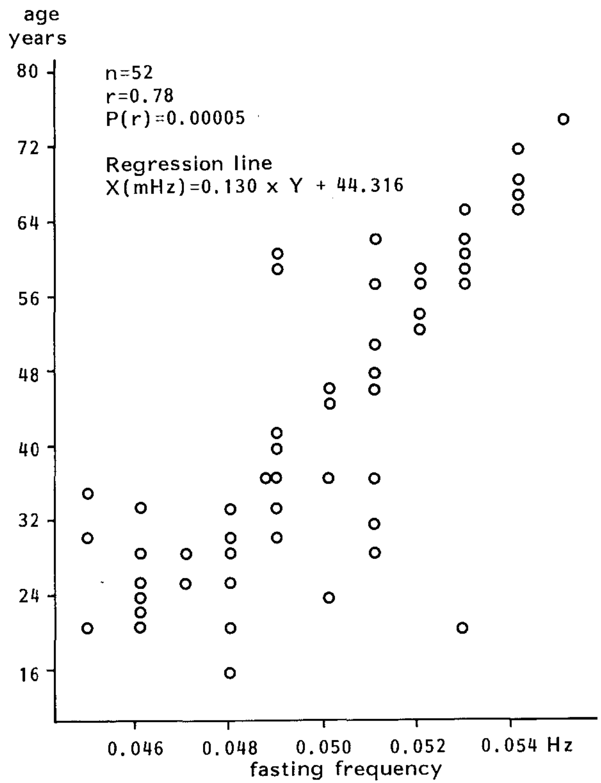


fig. 5.3.4 Schematic diagram defining the parameters of the postprandial frequency dip.

After the test meal an increase in the power of the gastric frequency was observed in all subjects. This is expressed by the power ratio (PR). Although the power of the gastric frequency increased at least a factor 2 after the test meal, the range of the PR indicates large inter-individual differences.


age
years
n=52
r=0.78
P(r)=0.00005
Regression line
X(mHz)=0.130 x Y + 44.316
80
72
64
56
48
40
32
24
16
0.046
0.048
0.050
0.052
0.054 Hz
fasting frequency

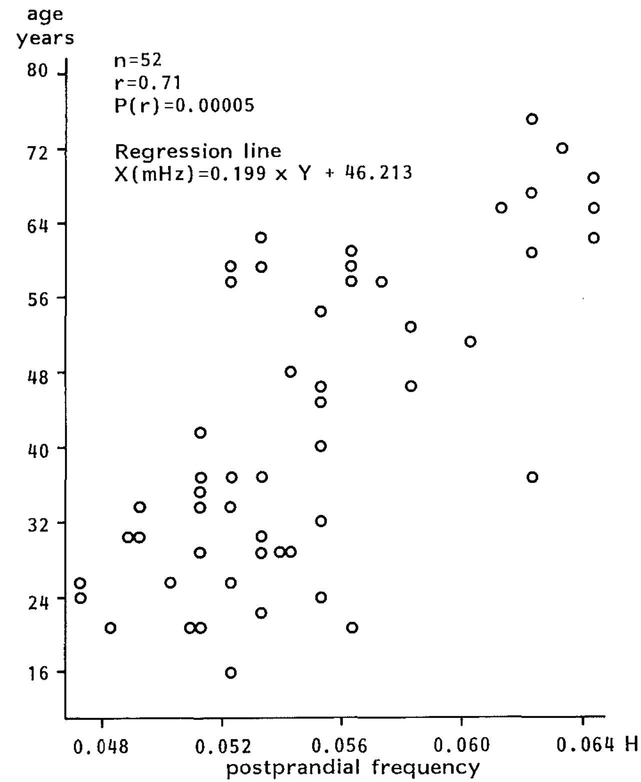

age
years
n=52
r=0.71
P(r)=0.00005
Regression line
X(mHz)=0.199 x Y + 46.213
80
72
64
56
48
40
32
24
16
0.048
0.052
0.056
0.060
0.064 Hz
postprandial frequency

fig. 5.3.5 Bivariate scatter plot of the correlation between the fasting gastric frequency and age.

fig. 5.3.6 Bivariate scatter plot of the correlation between the postprandial gastric frequency and age.

A second harmonic, the only parameter used in this study which is associated with the waveform of the electrogastrogram, was observed more often in the postprandial state.

Tachygastrias or other types of dysrhythmias were not seen in the control group.

A positive correlation was found between the gastric frequency and age. Both the fasting and the postprandial frequency increased with age (fig 5.3.5 and 5.3.6). In the fasting state: r=0.78, p=0.00005, regression line: fasting frequency (mHz)= 0.13 x age(yr) + 44.316. In the postprandial state: r=0.71, p= 0.00005, regression line: postprandial frequency (mHz)= 0.20 x age(yr) + 46.213. The remaining EGG parameters were not influenced by age, nor was there any correlation between sex and any EGG parameter.

The respiration signal was more often observed in the electrogastrogram during the postprandial state (82% of the recordings) than during the fasting state (24% of the recordings). This artefact was more frequently seen in men (men:women=3:1).

Frequencies compatible with the repetition frequency of the duodenal ECA were observed in only 2 of the 52 subjects.

5.3.4 Discussion

The values for the fasting and postprandial gastric ECA frequencies in our control population correspond with values reported in literature (8,23,53,75). The observed increase in the fasting and postprandial frequencies with age confirms the suggestion given by Smallwood based on his data in two small groups of healthy subjects but with a different age distribution (53). This positive correlation of the gastric ECA frequency with age explains the small differences found between the referred studies.

The control mechanism, motor correlate and the physiological function of the postprandial frequency dip, implicating a slowing-down of the gastric pacemaker rhythm, are not known nor understood. Since it is also unknown if the quantity and composition of the test meal influences the timing and frequency values of the dip, care should be taken in comparing data concerning the postprandial frequency dip. Nevertheless the values observed in our control population are in general agreement with the literature (14,45,75).

The normal postprandial power increase and thus an amplitude increase of the gastric frequency in the electrogastrogram is ascribed to the presence of ERA during motor activity (56,57,76,80). The large range of the power ratio (PR) can be partly explained by the different power levels in the interdigestive state. In section 5.2 we demonstrated that the power of the gastric frequency during phase II motor activity was a factor 2.61 (median) larger than during motor quiescence (phase I). Because the duration of the recording in the fasting state is relatively short (30 min.) in comparison to the duration of one interdigestive cycle (125 ± 22 min.) (46), the influence of the different power levels in the interdigestive state will be considerable and is probably one of the explanations for the large range of the PR.

The presence of a second harmonic of the gastric frequency in the spectrum is the only parameter used in this study that is directly associated with the waveform of the electrogastrogram. The more a periodic signal deviates from a sinusoid, the more harmonics may be expected to be present. Besides an increase in the power, ERA is also resonsible for a change in the waveform of the electrogastrogram (76,80) which explains the increased occurrence of second harmonics in the postprandial state in our control group. The underlying mechanisms of this phenomenon are still not well understood and further research in waveform analysis is necessary.

Respiration artefacts were frequently observed. However, after running spectral analysis the respiration frequency components are well separated from the gastric frequency components. As a consequence no interpretation problems arose. Visual inspection and analysis of an electrogastrogram contaminated with a respiration signal is impossible (2). This phenomenon illustrates once more the advantages of spectral analysis of the EGG signal. The finding that respiration artefacts were more often seen in men can probably be explained by the fact that 'abdominal respiration' is more common in men than in women.

In contrast to dogs, in humans the presence of duodenal frequencies in the electrogastrogram are extremely rare. The difference in anatomy between men and dog is probably one of the explanations.

5.4 EFFECTS OF GASTRIC BYPASS OPERATION AND SHAM FEEDING ON THE POSTPRANDIAL MYOELECTRICAL BEHAVIOUR

5.4.1 Introduction

Little is known about the control mechanisms of the postprandial motor- and myoelectrical behaviour. During the ingestion of a meal, the predominant motor activity is one of accomodation (31). With swallowing, the muscle fibers of the oral region of the stomach relaxe so that the material being swallowed can enter the stomach without causing much change in intragastric pressure. This mechanism, called receptive relaxation, is so efficient that the human stomach can accommodate approximately 2 litres of contents with a rise in pressure of less than 10 mm Hg. Receptive relaxation appears to be mediated by a neural reflex that has both its afferent and efferent pathways in the vagus nerves. This reflex is organized such that sectioning the vagus results in a less distensible stomach (29). Although a neural reflex is involved, neither the role of the intrinsic nerves nor the identity of the neurotransmitters involved are known. During the gastric phase of digestion of a meal the oral region exhibits mainly weak contractions (31). These contractions gently press the intragastric contents toward the caudal region. Much remains to be determined about the regulation of these tonic contractions, both neural and hormonal control has been suggested.

Much more is known about the control mechanisms of the rhythmic phasic, peristaltic, contractions exhibited by the distal part of the stomach after the ingestion of a meal. The timing and peristaltic nature of these contractions are regulated by the ECA which are generated intrinsically by the smooth muscle cells themselves (see section 2.3 and 2.5). The occurrence, timing and spread depend on the integrity of the gastric musculature, its innervation, and hormonal balance (5,30,31,section 2.5). When blood from a fed animal is perfused through an isolated stomach, the motility pattern of the isolated stomach resembles that seen in the stomach of the intact fed animal (30). The force of each contraction depends on the chemical composition of the gastric and duodenal contents and upon the physical characteristics of the gastric contents (49,82). For the control mechanisms responsible for the conversion into the postprandial motor activity pattern hormonal and neural pathways have been proposed. Distension of the corpus stimulates antral contractions via cholinergic pathways (4). Postprandial antral motor activity is reflected by an increase of the amplitude and a change in waveform of the electrogastrogram (sections 5.2 and 5.3).

With respect to the control mechanisms of the postprandial myoelectrical behaviour we were able to study a very interesting group of 'healthy' subjects undergoing gastric bypass surgery for obesitas. In these subjects the stomach was transsected in such a way that the content of the proximal stomach, connected to a jejunal loop, was about 100 ml. The vagal nerves were spared.

In addition the effect of sham feeding and of feeding by nasogastric tube on gastric myoelectrical activity by means of EGG was studied.

Objective of this study was to evaluate the response of gastric myoelectrical activity recorded by EGG to feeding after gastric bypass surgery and the response to sham feeding in order to obtain insight in the control mechanisms of postprandial myoelectrical behaviour.

5.4.2 Materials and methods

In the first part seventeen subjects, 5 men and 12 women (mean age 28, range 21-43) participated in the study. None of them had a history of any gastrointestinal or systemic disorder. The body weight of the subjects before operation varied between 84 and 185 kg with a mean of 114 kg. Three months after operation, at the time of the second recording the weigth varied between 72 and 106 with a mean of 88 kg. One patient died in the postoperative period.

Gastric bypass procedure. The stomach was transsected in such a way that the content of the proximal part of the stomach was about 100 ml. An end to end retrocolic gastrojejunostomy with a diameter of 12 mm and an end to side jejunojejunostomy (Roux en Y) was made. The vagal nerves were spared.

In the second part of the study gastric myoelectrical activity was studied (after an overnight fast) before, during and after sham feeding in 6 healthy male volunteers (mean age 25, range 19-40 yrs., body weight 68 $\pm$ 6 kg) without a history of any gastrointestinal or systemic disease. The subjects 'tasted and spit out' the same meal as used for standard electrogastrography described in section 4.4. The duration of the sham feeding was 5 minutes. In 4 of these 6 subjects the same standard meal was given by a nasogastric tube. Duration of feed administration was 5 min. Time between positioning of the tube and the feeding was 30 min. In contrast to the first part of the study (subjects sitting up while taking the test meal) in the second part of the study the subjects were lying down during the whole recording period. The test meal was given by one of the investigators to minimize motion artefacts.

The study was approved by the Medical Ethics committee of the Erasmus University, Rotterdam, on June 4, 1982 and carried out with the informed consent of the subjects.

The recording techniques are described in the sections 4.2 and 4.4. The methods used for signal analysis and data presentation are identical to that described in section 4.3.

Statistical analysis. The Wilcoxon signed-rank-test and the Fisher's exact test were used to evaluate whether a significant difference existed between the EGG parameters before and after gastric bypass procedure and before, during and after sham feeding. The level of significance used in this study was 0.05.

5.4.3 Results

Gastric bypass surgery. The results before and after gastric bypass surgery are summarized in the tables 5.4.1 and 5.4.2.

Table 5.4.1. EGG parameters before and after gastric bypass.

	before n = 14		after n=16	
	median	range	median	range
Fasting state				
Frequency (Hz)	0.048	0.045–0.051	0.046	0.043–0.050
Standard deviations (SD)	0.0028	0.0019–0.0036	0.0022	0.0016–0.0028
Instability factor (IF)	1.11	1.00–1.26	1.08	1.00–1.20
Second harmonics	35.7%		31.3%	
Postprandial state				
Frequency (Hz)	0.052	0.049–0.059	0.047*	0.043–0.052
Standard deviations (SD)	0.0026	0.0019–0.0036	0.0020	0.0017–0.0026
Instability factor (IF)	1.05	1.00–1.24	1.06	1.00–1.18
Second harmonics	64.3%		37.5%*	
Power ratio (PR)	3.86	2.09–10.09	1.12*	0.75–1.44

The presence of second harmonics is expressed in %.
p-value for the difference between the groups: * p = 0.01.

Table 5.4.2. Frequency dip parameters before and after gastric bypass.

		before n=14		after n=16	
		median	range	median	range
F_{max}	(Hz)	0.054	0.045–0.060	0.053	0.046–0.059
F_{min}	(Hz)	0.038	0.036–0.041	0.042*	0.039–0.044
T_{max}	(min)	11	7–14	12	7–14
T_{min}	(min)	3	2–4	4	2–5
T_d	(min)	8	5–11	9	6–12
T_s	(min)	5	4–8	5	4–9

p-value for the difference between the groups: * p=0.01.

Three of the recordings before surgery could not be interpreted after running spectrum analysis because of a very poor signal to noise ratio. The quality of the recordings after the operation, and thus after a considerable lost of weight, was better. However, the signal to noise ratio was in general less than in the control population (section 5.3) and the motion artefacts were more severe, in particular during feeding, making interpretation of the EGG during feeding unreliable.

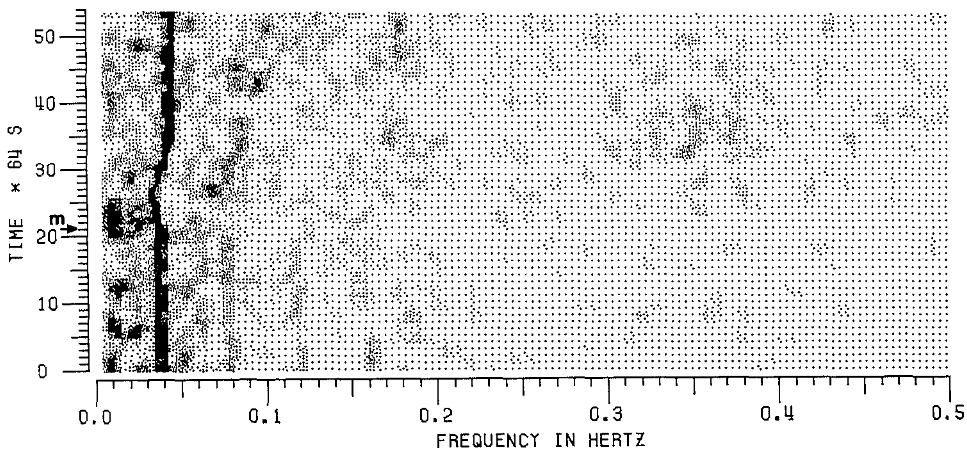


fig. 5.4.1 Grey-scale plot of an electrogastrogram after gastric bypass surgery. The frequency and power behaviour is characteristic for this group. Note the less pronounced frequency dip and the absence of the power increase following the ingestion of the test meal marked with a 'M'.

After gastric bypass surgery three remarkable changes in gastric myoelectrical activity were found: 1) Absence of the normal postprandial power increase, 2) A low percentage of higher harmonics in the postprandial state, 3) A less pronounced frequency dip (higher F_{min}), 4) No postprandial increase in the gastric frequency. The grey-scale plot in figure 5.4.1 is representative for the abnormalities found.

Another remarkable finding after operation was the presence in 7 subjects of a very stable frequency at about 4-5 times higher than the gastric frequency and obviously different from the respiration frequency. This frequency which showed no changes after food intake could well be of small intestinal origin.

Sham feeding. In the second part of the study the fasting gastric frequency ranged between 0.047 and 0.050 Hz, with a median of 0.049 Hz. After sham feeding the changes in myoelectrical behaviour were limited to a period during and shortly (5 min.) after sham feeding.

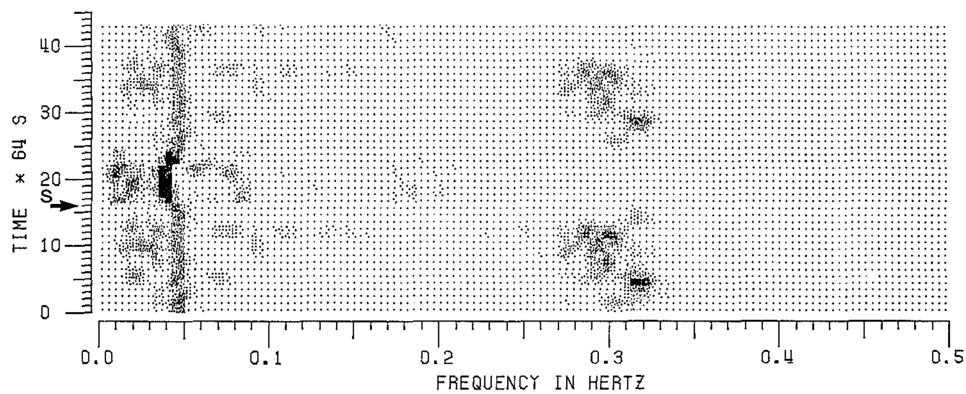


fig. 5.4.2 Grey-scale plot of the electrogastrogram before, during and after sham feeding. Note the small power increase and the abrupt small frequency decrease only present during sham feeding marked with 'S'.

A small but significant power increase ($p<0.05$) was found during sham feeding ranging from 2.64 to 4.26, with a median of 3.53. A small frequency decrease was observed ranging between 0.004 and 0.008 Hz. The frequency decrease started 1-3 min after sham feeding and lasted for maximal 5 min and was quite different from the normally observed frequency dip (fig. 5.4.2). The subsequent myoelectrical behaviour was not significantly different from the fasting period.

Tube feeding. The frequency and power level in the fasting state was in this recording session identical to the values reported in the sham feeding experiment. After starting the administration of the test meal via a tube a small frequency decrease was found, but this frequency decrease was also different from the frequency dip observed in normal subjects. One to three min. after starting the tube feeding the frequency jumped to a value 0.004-0.0010 Hz below the fasting frequency. Duration of this 'frequency dip' was maximal 6 min. Subsequently the frequency stabilized at a level which was in general somewhat higher (0.002-0.004 Hz) than the fasting frequency In contrast to sham feeding a prolonged power increase was observed after 'tube feeding' ranging from 3.87 to 6.96, with a median of 5.78 (fig. 5.4.3).

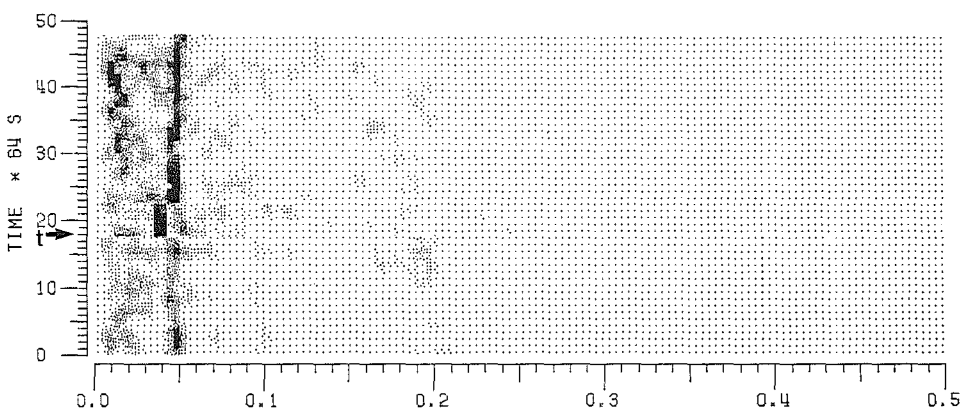


fig. 5.4.3 Grey-scale plot of the electrogastrogram before, during and after 'tube feeding'. Note the small postprandial power increase and the 'jump' to a somewhat lower frequency following the start of 'tube feeding' marked with 'T'.

5.4.4 Discussion

The values of the EGG parameters in the studied groups before gastric bypass surgery and before sham feeding are, considering the different age distributions, in agreement with values found in the control population (section 5.3).

The bad signal to noise ratio was probably due to the marked obesity resulting in problems with finding the right position for the electrodes and attaching them. In addition the very mobile panniculus aggravated the motion artefacts.

The normally observed postprandial power increase and the increase in percentage of higher harmonics has been argued to be a reflection of the postprandial motor activity (section 5.3). The absence of the postprandial power increase and low, almost equal to the fasting state, percentage of higher harmonics in the postprandial state after gastric bypass surgery indicates that conversion to the normal postprandial motor activity does not occur and that the presence of food in the stomach is essential for this conversion. Another explanation for the absence of the conversion to a postprandial motility could be a negative feedback from the small intestine. After gastric bypass surgery the chyme reaches the small intestine very quickly. It is therefore important to realize that the antral motor activity in these subjects could be inhibited by distention of the small intestine by the test meal (21) or by the physico-chemical composition the test meal (26,49). However, these mechanisms normally modulate antral motor activity and it is unlikely that they abolish postprandial motor activity totally. The small power increase during sham feeding is in agreement with the results of Stern et al (65) and suggest the presence of antral contractile activity during cephalic-vagal stimulation. Apparently cephalic-vagal stimulation itself is not sufficient to evoke postprandial phasic antral motor activity. The finding that after 'tube feeding' a power increase was observed resembling the normal postprandial power increase supports the hypothesis that the presence of food in the stomach is essential in initiating postprandial antral motor activity. This is in agreement with literature (4). No effect on antral motor activity can be expected from the test meal in the small oral part of the stomach after transection because it is known that transsection of the enteric nervous system which is intrinsic to the wall of the gastrointestinal tract (Auerbach's plexus and Meissner's plexus), abolishes the effect of distension of the oral part of the stomach on motor activity (4).

The control mechanism of the postprandial frequency behaviour remains unclear, although this study suggests that the presence of food in the stomach is a prerequisite for a postprandial frequency at a somewhat higher level than the fasting frequency. A small frequency decrease was observed during and after sham feeding the character of this 'frequency dip' was quit different from the dip observed in normal controls making cephalic-vagal stimulation as major control mechanism unlikely. The frequency dip during and after 'tube feeding' was also quit different and in fact resembled the frequency changes after sham feeding. However, the frequency dip after gastric bypass surgery, although less pronounced than is normally observed, resembled the normally observed dip. The initial postprandial frequency behaviour apparently is determined by many control mechanisms. The almost normal frequency dip found after gastric bypass surgery supports the hypothesis that hormonal control, hormones released by the chyme in the small intestine, could be very important in controlling the postprandial frequency behaviour (31). It is namely unlikely that the food in the proximal gastric remnant is responsible for a neurally mediated dip in these patients, because the enteric nervous system between the oral part of the stomach (and the adjacent small intestine) containing the food and the distal part of the stomach and duodenum is transsected.

In conclusion: 1) The number of motion artefacts is markedly increased in obesity, sometimes making interpretaion of the electrogastrograms impossible. 2) Cephalic-vagal stimulation does not evoke postprandial antral phasic contractions. 3) The presence of food in the stomach is necessary for the induction of postprandial antral motor activity. 4) This study does not allow firm conclusions to be drawn on the regulation of the postprandial frequency behaviour. The changes in frequency seen after administration of food possibly have many control mechanisms.

6. Electrogastrography in patients

6.1 GASTRIC MYOELECTRICAL DISTURBANCES IN THE FASTING AND POSTPRANDIAL STATE IN GASTRIC ULCER PATIENTS: AN ELECTROGASTROGRAPHIC STUDY

Submitted for publication.
Co-authors E.J. van der Schee, J.P. van de Merwe, M. van Blankenstein, J.L. Grashuis.

6.1.1 Abstract

This study of gastric ulcer patients examined whether characteristic disturbances in the fasting and postprandial gastric myoelectrical activity could be discerned electrogastrographically. A total of 61 recordings were made in 31 gastric ulcer patients, both at the time of diagnosis and after ulcer-healing, and 52 recordings were made in 52 control subjects. Several types of abnormal gastric myoelectrical activity were found in patients with an active ulcer: 1) instability of both the fasting and postprandial gastric frequency; 2) the absence of the normal postprandial amplitude increase in the electrogastrogram; 3) waveform changes in the electrogastrographic signal both in the fasting and postprandial state; 4) tachygastrias.

Abnormal gastric myoelectrical activity was predominantly found in association with symptoms of nausea and vomiting and was not merely due to the presence of the ulcer itself.

6.1.2 Introduction

Motility in the stomach depends on the electrical activity of the smooth muscles. Abnormalities in this myoelectrical activity may be associated with motility disorders, and could thus be of diagnostic significance.

In man cyclic recurring electrical potentials, referred to as electrical control activity (ECA) (1), originate in the oral part of the corpus and travel aborally through the longitudinal muscle fibers to the pylorus. This constantly present ECA is generated at intervals of about 20s, which corresponds with a repetition frequency of about 0.05 Hz. When phasic contractions occur, the ECA is accompanied by a second component with or without superimposed fast oscillating potential changes, which is referred to as electrical response activity (ERA) (1).

Little is known about the pathophysiology of gastric myoelectrical activity. Dysrhythmias and changes in ECA frequency have been described in patients after vagotomy (2-5). In gastric ulcer patients both abnormally high frequencies and arrhythmias (6,7,8) and normal frequencies have been observed (9,10). Similar contradictory results have been found in patients with gastric carcinoma (7-10). The study of Fioramonti and Bueno is of particular interest (11). In rats and dogs with experimentally induced gastric ulcerations they observed a disorganisation of the fasting myoelectrical pattern and a decrease in amplitude of the postprandial fast oscillating potentials. It has recently been suggested that there is a relationship between symptoms of disordered gastric motility and abnormal gastric myoelectrical behaviour (12-14). This behaviour was characterized by episodes of increased (2-4 times) ECA frequency, which is referred to as tachygastrias or tachyarrhythmias, and was seen in the fasting state in some patients with chronic unexplained nausea and vomiting. Tachygastrias can, however, also occur in the absence of any gastric symptoms (5).

Most of the above studies were performed either with peroral (suction) electrodes or with serosal electrodes placed during laparotomy and recordings were only made in the fasting state. However, invasive methods are not very suitable for the study and follow up of large groups of patients.

Gastric myoelectrical activity can, however, be recorded in a noninvasive way by means of electrodes attached to the abdominal skin. This method is known as electrogastrography (EGG) and the recorded signal as an electrogastrogram. EGG allows the recording of gastric myoelectrical activity in both the fasting and postprandial state, providing information about normal and disturbed ECA frequencies, such as tachygastrias (15-21). The amplitude of the EGG signal increases at the onset of ERA and is an indication of contractile activity (15,22). Running spectrum analysis in combination with a grey-scale plot or a pseudo-3-dimensional plot, allows a quick visual interpretation of the EGG data which means that among other things even tachygastrias of short duration, can be detected (23).

In the present study, EGG was performed in gastric ulcer patients to investigate whether characteristics variations in the normal frequency and power pattern of the electrogastrogram could be discerned and whether these abnormalities were related to ulcer characteristics (location and size) and complaints of nausea and vomiting. In addition we examined to what extent the myoelectrical behaviour returned to normal after ulcer-healing.

6.1.3 Materials and methods

Subjects. Thirty-one gastric ulcer patients (17 males and 14 females, median age 52 years, range 32 - 68) participated in the study. All patients were studied within 3 days of gastroscopy which had demonstrated an active untreated ulcer crater. Patients with evidence of stricture of mechanical obstruction in combination with an ulcer crater were excluded from the study which means that ulcers that were directly prepyloric were excluded. Other exclusions criteria were a history of systemic illness (e.g. vasculitis, diabetes mellitus), neurological disorders, duodenal ulcer, malignant gastric ulcer, reflux oesophagitis, previous gastro-intestinal or biliary surgery and concomitant disease predisposing to stress ulceration. Patients taking any drug were also excluded from the study. Seventeen ulcers were located along the lesser curvature, 8 along the greater curvature in the corpus and oral part of the antrum, and 6 near the cardia. All ulcers were single, ranging in diameter from 1 to 4 cm. Eighteen patients complained of nausea, and two or more of the following symptoms: belching, abdominal distension, sense of fullness after a normal meal, inability to finish a normal meal, and vomiting (with or without pain and/or bleeding). These symptoms were also present on the day of the recording and thus during the recording. In the other 13 patients the presenting symptoms were limited to pain and/or bleeding. (In this study the 18 patients will be referred to as patients with nausea and vomiting.) Thirty patients (one patient died following rebleeding) were studied again within 7 days of gastroscopy which had shown total ulcer healing. Fifteen patients had been treated with an H2 receptor-antagonist (cimetidine), 14 with colloidal bismuth citrate and one with antacids. Ulcer treatment was stopped at least 7 days before the recording. All 30 patients were free of complaints at the time of this second recording, 6 - 10 weeks after the initial recording.

Control subjects were 27 men and 25 women with a median age of 42 years, range 16 - 75, without a history of gastro-intestinal or systemic disorder.

The study was approved by the Medical Ethics committee of the Erasmus University, Rotterdam, on June 4, 1982 and was carried out with the informed consent of the subjects.

Technique of recording. Although in most subjects an optimal electrode direction coincides with the antral axis (24), the optimum electrode position cannot be defined exactly because of interindividual anatomical variations (25,26). Therefore several leads were used and the signal with the best signal to noise ratio was then selected for further analysis. In this choice contamination of the signal with a respiration component is of less importance than are large motion artefacts, which occur in particular in the monopolar leads. The positions of the 6 recessed-type electrodes (Red Dot 2256, 3M Co.) used in this study are shown in fig. 6.1.1. The shield electrode is used to reduce possible interference from the 50 Hz mains voltage at the input stage of the preamplifiers.

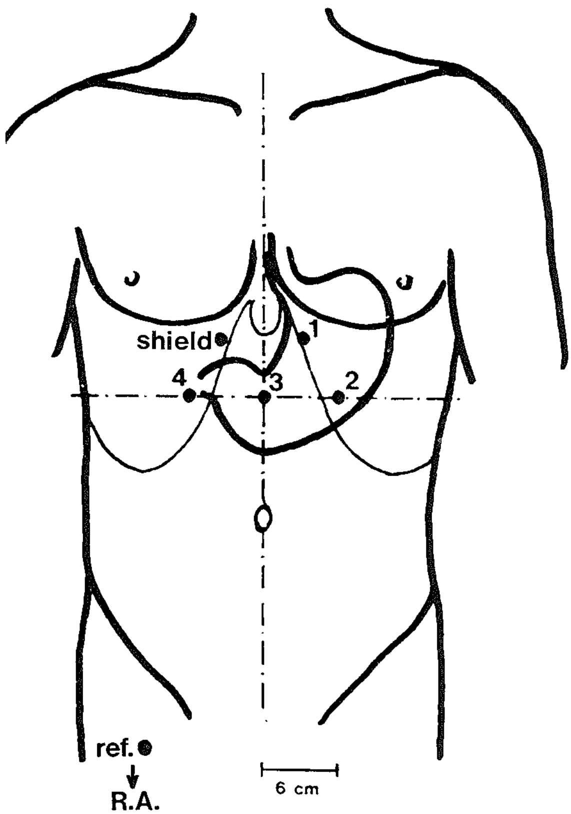


fig. 6.1.1 Electrode positions used in this study. Electrodes 2, 3 and 4 are situated on a transverse line halfway between the lower end of the sternum and the umbilicus. Electrode 3 is placed at the intersection of this line and the median plane. Distance between all abdominal electrodes is 6 cm. Reference electrode is on the right ankle (R.A.).

A strain gauge respiration transducer was attached to the thoracic wall. Myoelectrical activity during fasting was recorded for a 30 min period after an overnight fast. A test meal consisting of 250 ml of yoghurt with 20 g of sugar was then given, and consumed within 4 min, while the recording was continued. The composition of the test meal was: 990 kJ, 8.75 g protein, 8.75 g fat and 30 g carbohydrate. The recording was stopped 35 min. after the start of the test meal. Subjects lay quietly in a supine position during most of the recording session (only sitting up while taking the test meal). The 4 monopolar and 6 bipolar signals were recorded on paper (Van Gogh EP-8b) and simultaneously stored on magnetic tape (Racall Store 14). The high- and low-pass filters (6 decibel/octave) were set at 0.01 and 0.5 Hz respectively (25).

Signal analysis. A fast Fourier transform algorithm implemented on a NOVA 2 digital computer was used to obtain power spectra of the time signals. The signals, replayed from tape 16 times faster than real time, were preprocessed by band-pass filtering using a Butterworth filter (24 decibel/octave) with (real time) cut-off frequencies set at 0.01 and 0.5 Hz, to remove possible DC components and to avoid aliasing. They were then digitized (real time sampling frequency 1 Hz) and fed into the computer. The time signal of the whole recording period was used for signal analysis. Spectra were obtained as follows: every 64 s a power spectrum was computed from the preceeding 256 s of the EGG time-signal, to which a Hamming window was applied to reduce leakage (27). These time values have been shown to enable the extraction of relevant information from the EGG, giving 129 points per spectrum and a frequency spacing of 0.0039 Hz (23). Tachygastrias which have a duration of at least 64 s can be detected using these time values (23). This procedure generates series of spectra that overlap in time, called running spectra. They were plotted in two different ways, using pseudo-3-dimensional and grey-scale plots (fig. 6.1.2 and 6.1.3). The grey-scale plot enables the easy recognition of frequency changes in course of time. In the grey-scale plot the blackness is proportional to the magnitude of power of the EGG-signal, divided into 36 distinct grey levels. However, power- and thus amplitude changes (amplitude is the square root of the power) can be recognized more precisely in the pseudo-3-dimensional plot. Plots were made on a Versatec 1100 A printer plotter.

During processing each computed spectrum was drawn, with its spectrum number, on a Tektronix 4010 display terminal with hard copy facilities. Where there were problems of interpretations after completion of the processing each spectrum could be analysed in detail. The mean gastric frequency (Hz), with standard deviation (SD), and its power content were computed for both the fasting and postprandial states. To give a measure of the variability in the ECA frequency variations visible in grey-scale plots (see e.g. fig. 6.1.6) we introduced a new parameter, called the Instability Factor (IF). This was defined as the ratio of the frequency standard deviation of the whole fasting or postprandial period to the frequency SD of one, arbitrary chosen, spectrum containing a clearly present gastric frequency component in the fasting or postprandial state respectively. When no frequency variations are present the IF will be 1. The larger the IF, the more the gastric frequency did vary and thus the more unstable was the gastric frequency in the period analyzed.

Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance to the stomach wall), it is impossible to make a comparison of inter-individual and even intra-individual absolute values of power data in separate recordng sessions Therefor in this study only power changes in one single recording session were used for analysis. To quantify the postprandial power change, the ratio of the power of the gastric frequency component in the postprandial state to the power of the gastric frequency component in the fasting state was computed and referred to as the Power Ratio (PR). A PR>1 indicates a postprandial increase of the power of the gastric frequency component, a PR<1 a postprandial power decrease.

Where it was considered to be necessary running spectrum analysis of the respiration signal was performed to exclude confusion between frequencies of respiratory origin and possible tachygastrias.

The only parameter used in this study that was associated with the electrogastrographic waveform, was the presence of a second harmonic of the gastric frequency in the spectrum. The more a periodic signal deviates from a sinusoid, the more harmonics may be expected to be present. Higher harmonics can be recognized in the spectrum because their frequency spacing forms exactly an integer. A second harmonic of the gastric frequency was considered to be present if its power amounted to at least 5% of the power of the first harmonic, i.e. the gastric frequency itself.

Statistical analysis. Dichotomized data were compared with the Fisher's exact test. To compare continuous data between groups the Mann-Whitney U-test (non-parametric) was used. Paired results (patients with an active ulcer compared with the same patients after healing) were evaluated using the sign-test (dichotomized data) and Wilcoxon's signed-rank-test (continuous data). Regression lines (least square method) and coefficients of correlation (r) were calculated for normally distributed data, otherwise the Spearman rank correlation test was used. Probability (p) values were derived from two-tailed tests.

6.1.4 Results

A total of 113 standard recordings were made in the 83 patients and controls. In the control group 4.7% of the total recording time after running spectrum analysis (the initial 2-4 spectra after food intake) could not be interpreted, because of motion artefacts due to the food intake. In the ulcer group 7% of the recording time could not interpreted after running spectrum analysis because of motion artefacts due to food intake and vomiting in the postprandial phase. After ulcer-healing this percentage was reduced to 4.2%, due to motion artefacts caused by food intake only.

In 54% of the cases lead 1-4 and in 30% lead 2-3 was used for signal analysis. In the remaining cases the leads 1-3 or 2-4 were used. Seventy-four statistical tests were carried out on the results and in table 6.1.1 it can be seen that the number of observed statistically significant results is much higher than expected by chance when 0.05 is taken as the critical significance level.

Table 6.1.1. Cumulative numbers of expected and observed tests with statistical significance in ulcer patients.

Significance level	expected	observed
p<0.05	3.7	26
p<0.025	1.85	21
p<0.01	0.74	17
p<0.005	0.37	11
p<0.0025	0.185	11
p<0.001	0.074	10
p<0.0005	0.037	9
p<0.00025	0.0185	8
p<0.0001	0.0074	8
p<0.00005	0.0037	6

Total number of tests 74.

Control Group (table 6.1.2). During the fasting state a pattern of relatively low power magnitude was observed. The small instability factor (IF), i.e. close to 1, confirmed the impression obtained by visual inspection of the computed plots that the fasting frequency was stable (fig. 6.1.2 and 6.1.3). Immediately after the test meal a "frequency-dip" was seen in every subject. The average frequency decrease was 23% of the fasting frequency. After about 5 min. the frequency started to increase again and generally rose to a temporarily higher level (fig. 6.1.3). After that the frequency, referred to as the postprandial frequency, stabilized at a level which was at least equal to or somewhat higher than the fasting frequency.

The power magnitude of the EGG-signals expressed by the power ratio (PR) increased after the test meal, by at least a factor 2 (PR>2) (fig. 6.1.2). However, large inter-individual differences were observed. A second harmonic was more often found in the postprandial state than in the fasting state. Frequencies compatible with tachygastrias (a frequency 2-4 times higher than the normal gastric frequency while the normal gastric frequency is absent) were not seen in the control group.

Table 6.1.2. Statistics of EGG parameters in ulcer patients and control group. Results are expressed as median and range, except for the second harmonic.

	Ulcer patients		Control group	
	active ulcer	after healing		Level of significance (p) between groups
	n=31 (U)	n=30 (H)	n=52 (C)	U-H-C
Fasting state				
Frequency (Hz)	0.051 0.045–0.065	0.050 0.044–0.055	0.050 0.045–0.055	U-C: n.s. U-H: n.s. H-C: n.s.
Instability factor (IF)	1.15 1.00–1.86	1.11 1.00–1.36	1.12 1.00–1.40	U-C: n.s. U-H: p = 0.04 H-C: n.s.
Second harmonic (%)	71	36.6	38.5	U-C: p = 0.008 U-H: p = 0.02 H-C: n.s.
Postprandial state				
Frequency (Hz)	0.052 0.042–0.062	0.054 0.047–0.064	0.054 0.047–0.064	U-C: p = 0.04 U-H: p = 0.05 H-C: n.s.
Instability factor (IF)	1.38 1.00–4.57	1.18 1.00–1.41	1.10 1.00–1.40	U-C: p = 0.00005 U-H: p = 0.0001 H-C: n.s.
Second harmonic (%)	35.5	66.6	67.3	U-C: p = 0.009 U-H: p = 0.02 H-C: n.s.
Power ratio (PR)	2.17 0.21–12.15	3.13 1.63–11.49	6.79 2.08–16.61	U-C: p = 0.00005 U-H: p = 0.01 H-C: p = 0.008

n.s. = not significant ($p > 0.05$).

The frequency during fasting increased with age ($r = 0.78$; $p = 0.00005$; regression line: fasting frequency (mHz) = 0.130 x age (yr) + 44.316). The postprandial frequency also increased with age ($r = 0.71$; $p = 0.00005$; regression line: postprandial frequency (mHz) = 0.199 x age (yr) + 46.213). The remaining EGG-parameters were not influenced by age. There was no correlation between sex and EGG-parameters.

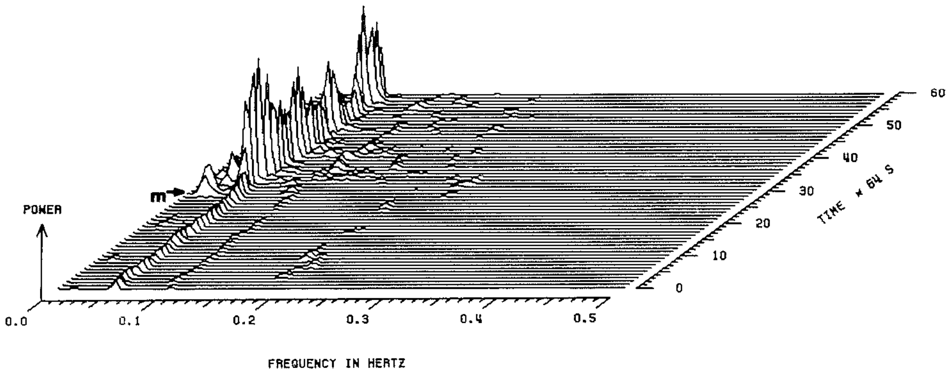


fig. 6.1.2 Pseudo-3-D display of the electrogastrogram of a control subject. Note the power increase after the test meal marked by an "M'. A second harmonic is present at 0.10 Hz.

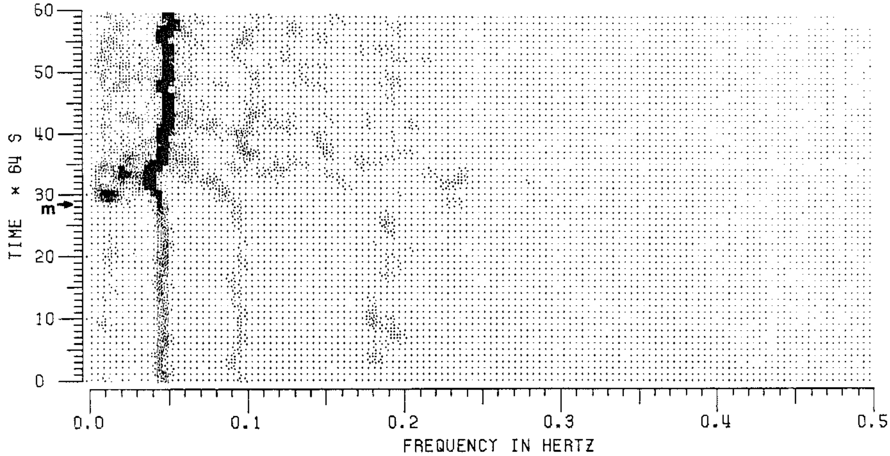
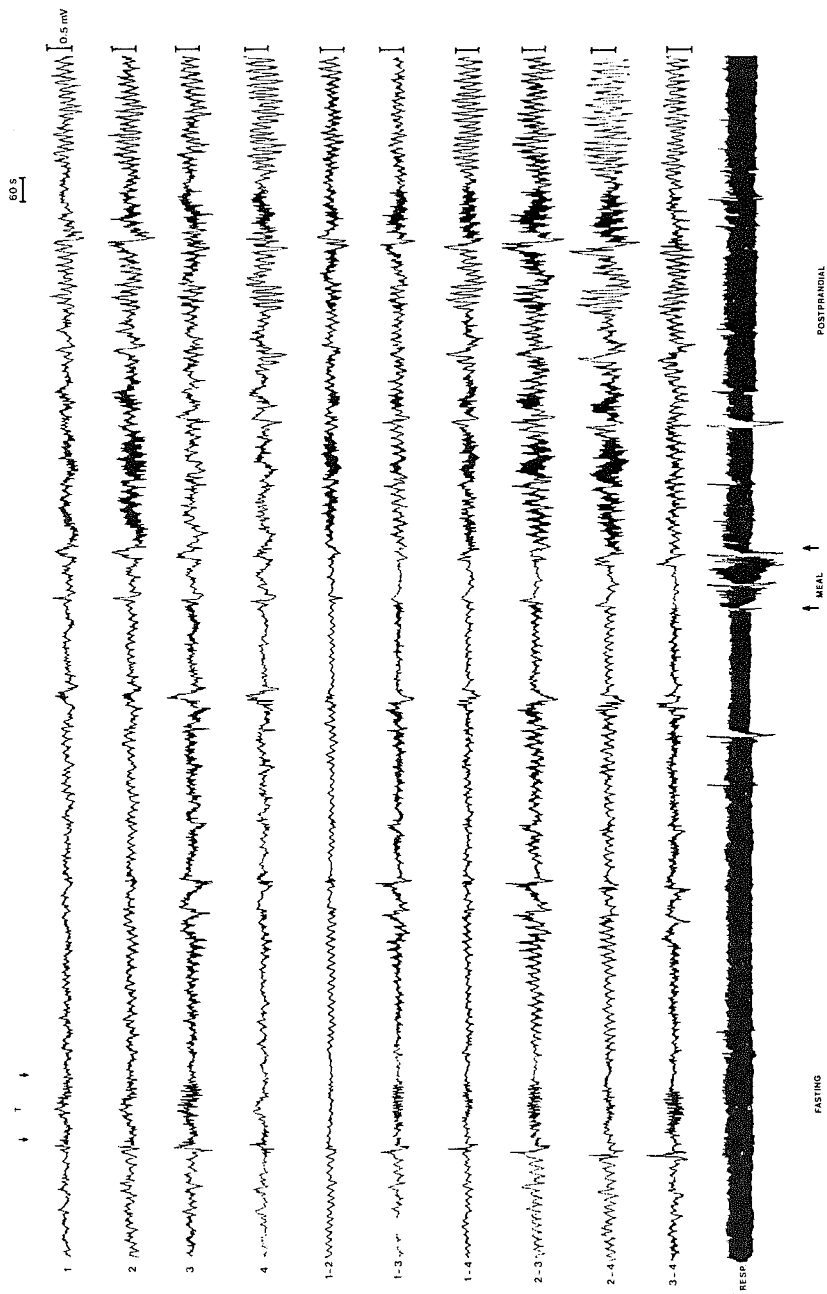


fig. 6.1.3 Grey-scale plot of the electrogastrogram of the same control subject as in fig. 6.1.2. Note the frequency-dip following the ingestion of a test meal marked with "M".



0.5 mV
60 s
T
1
2
3
4
1-2
1-3
1-4
2-3
2-4
3-4
RESP.
FASTING
MEAL
POSTPRANDIAL

fig. 6.1.4 The 10 (4 monopolar, 6 bipolar) time signals of an ulcer patient with a tachygastria in the fasting state. (Only part of the postprandial recording is shown.) Signal 2-3 is chosen for further analysis and the corresponding grey-scale plot is shown in fig. 6.1.5. "T" indicates the period of tachygastria. Bottom trace is the respiration signal. Parts of the postprandial signals are contaminated with respiration artefacts.

Ulcer group. Fasting state (table 6.1.2 and 6.1.3). The frequency during fasting in ulcer patients was not significantly different to that in the control group. The IF in this group showed a larger range, indicative of a less stable fasting frequency. An increased IF only occurred in patients with nausea and vomiting. This subgroup showed a significant difference, when compared with patients without nausea and vomiting and with the control group. After ulcer-healing the IF in this group returned to values identical to the control group.

The percentage of second harmonics in the fasting state was higher in the ulcer group than in the control group, mainly due to a significantly higher percentage in patients with nausea and vomiting. After ulcer-healing a shift towards normal was seen.

Frequencies compatible with tachygastrias were found in 4 patients and lasted 3,5,7 and 10 min. respectively (fig. 6.1.4 and 6.1.5). They had all complained of nausea and vomiting. Tachygastrias were not observed after ulcer-healing.

Ulcer group. Postprandial state (table 6.1.2 and 6.1.3). The postprandial frequency in ulcer patients was lower than in the control group. This difference was due to the patients with nausea and vomiting, there being a significant difference between this subgroup on the one hand and patients without these complaints and the control group, on the other. After ulcer-healing a shift towards normal was found.

Table 6.1.3. Statistics of EGG parameters in ulcer patients divided in two groups, i.e. patients with and without nausea and vomiting. Results are expressed as median and range, except for the second harmonic.

	Ulcer patients (active ulcer)		Control group	
	without nausea and vomiting n=13 (O)	with nausea and vomiting n=18 (NV)	n=52 (C)	Level of significance (p) between groups O-NV-C
Fasting state				
Frequency (Hz)	0.052 0.049–0.060	0.049 0.045–0.065	0.050 0.045–0.055	O-NV: n.s. NV-C: n.s. O-C : n.s.
Instability factor (IF)	1.10 1.00–1.40	1.15 1.00–1.86	1.12 1.00–1.40	O-NV: p = 0.02 NV-C: p = 0.02 O-C : n.s.
Second harmonic (%)	46.2	88.9	38.5	O-NV: p = 0.03 NV-C: p = 0.001 O-C : n.s.
Postprandial state				
Frequency (Hz)	0.055 0.049–0.060	0.049 0.042–0.062	0.054 0.047–0.064	O-NV: p = 0.002 NV-C: p = 0.001 O-C : n.s.
Instability factor (IF)	1.24 1.00–1.42	2.20 1.34–4.57	1.10 1.00–1.40	O-NV: p = 0.0001 NV-C: p = 0.00005 O-C : n.s.
Second harmonic (%)	61.5	16.7	67.3	O-NV: p = 0.03 NV-C: p = 0.00009 O-C : n.s.
Power ratio (PR)	2.85 1.88–12.15	0.34 0.21–7.85	6.79 2.08–16.61	O-NV: p = 0.0005 NV-C: p = 0.00005 O-C : n.s.

n.s. = not significant ($p > 0.05$).

Marked variations (fig. 6.1.6) in the postprandial frequency were often observed, as expressed by the increased IF in ulcer patients. These frequency variations (IF>2.00), however, only occurred in patients with nausea and vomiting (fig. 6.1.9). After ulcer-healing the IF returned towards normal.

Another remarkable finding was the low PR in ulcer patients. There was even a power decrease (PR<1.00) after the test meal in 11 patients (fig. 6.1.7, 6.1.8 and 6.1.10). There was again an interesting difference between the subgroups. In patients without nausea and vomiting PR values fell in the same range of the control group. After ulcer-healing the PR for the nausea and vomiting subgroup increased significantly but did not always quite achieve control levels, although there was always a power increase (PR>1.00) postprandially (fig. 6.1.10).

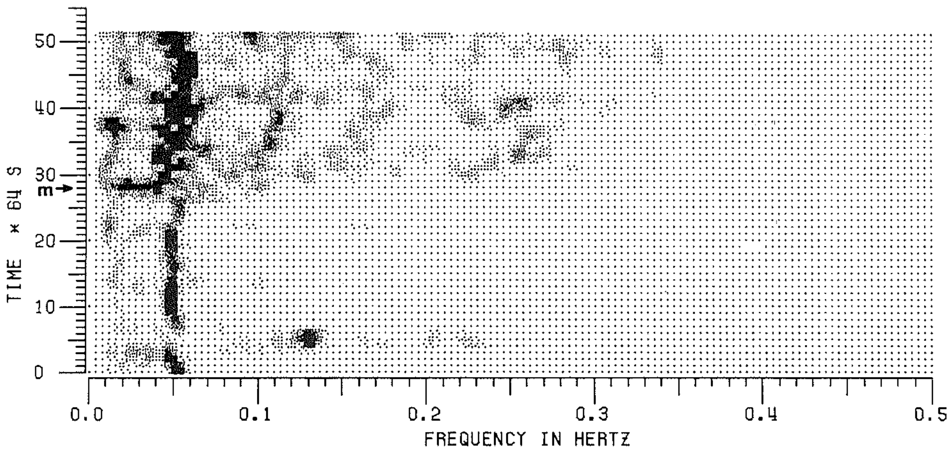


fig. 6.1.5 Grey-scale plot of the EGG shown in fig. 6.1.4. The tachygastria with a frequency of about 0.13 Hz is present in the fasting state. Note the absence at that moment of the normal gastric frequency at about 0.05 Hz. The unstable frequency in the postprandial state is not clearly visible because the grey level chosen to show the tachygastria clearly, gives an excessive blackness in the postprandial phase. Due to the unstable postprandial frequency the second and third harmonic at about 0.11 Hz and 0.17 Hz respectively are also unstable. The frequencies between 0.20 and 0.30 Hz are of respiratory origin.

Whereas the percentage of second harmonics in the fasting state in the control group was low, this percentage was high in the ulcer group, reaching the "postprandial" value of the control group. It then fell in the postprandial state to a percentage which was below that observed in fasting controls. The incidence of second harmonics was significantly lower in patients with nausea and vomiting than in patients without these complaints. After ulcer-healing the incidence of second harmonics increased, becoming almost identical to that of the control group.

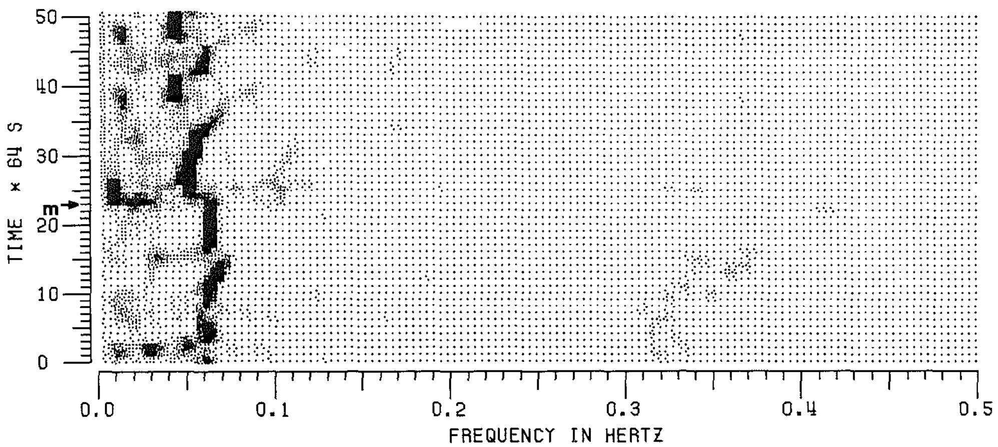


fig. 6.1.6 Grey-scale plot of an electrogastrogram of a patient with an active ulcer. In particular in the postprandial state wide frequency variations are present (IF = 3,26). "M" indicates the start of the test meal.

In the postprandial state no frequencies compatible with tachygastrias were observed in ulcer patients either before or after ulcer healing.

No significant correlation or trend was present between fasting and/or postprandial EGG-parameters and ulcer characteristics (location and size). There was no significant correlation with age, either, even though the fasting and postprandial frequency after ulcer-healing tended to increase with age.

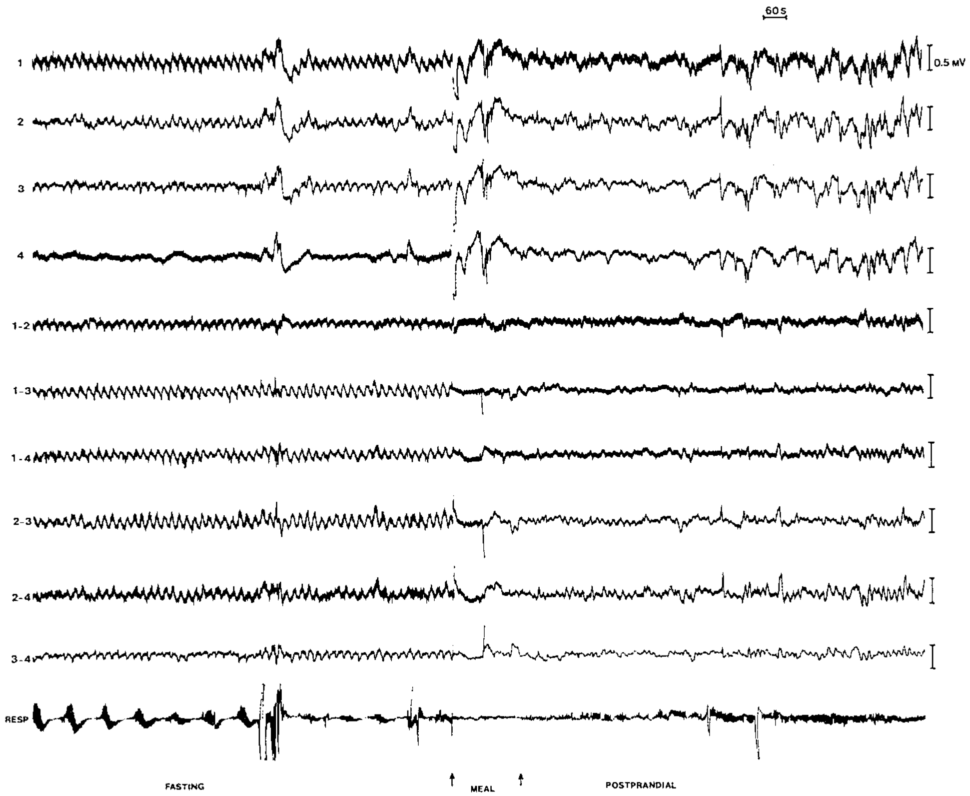


fig. 6.1.7 The 10 (4 monopolar, 6 bipolar) time signals of an ulcer patient with a postprandial amplitude decrease. (Only part of the recording shortly before and after the test meal is shown.) Signal 1-4 is chosen for further analysis and the corresponding pseudo-3-D display is shown in fig. 6.1.8. Bottom trace is the respiration signal.

6.1.5 Discussion

Information on motility in gastric ulcer patients is limited but there is evidence that gastric emptying is delayed (28,29), and an increased duodenal-gastric reflux is present (28,30). As the control mechanism of motility is of an electrical nature, focussing attention on gastric myoelectrical behaviour in these patients may be of great importance. This study has used electrogastrography to measure the myoelectrical behaviour of the stomach in ulcer patients and in a control group.

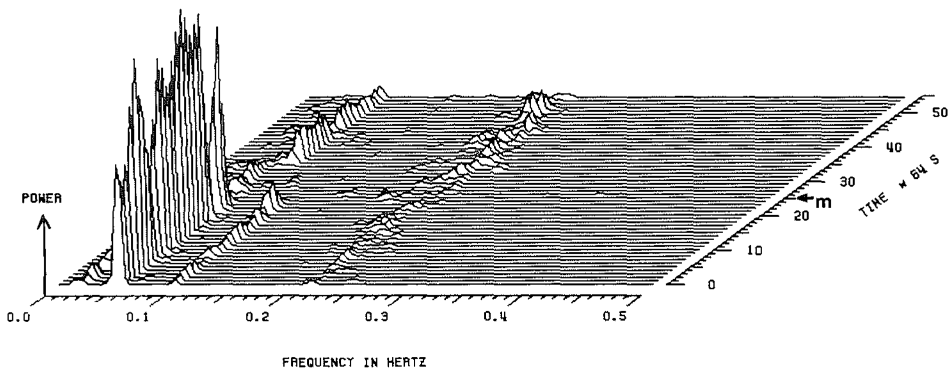


fig. 6.1.8 Pseudo-3-D display of the electrogastrogram shown in fig. 6.1.7. Note the power decrease in the postprandial state (PR = 0.35) and the second harmonic present in the fasting state at 0.10 Hz. Frequencies at about 0.22 Hz are of respiratory origin. "M" indicates the start of the test meal.

In the control group the gastric ECA frequencies, both in the fasting and the postprandial states, are in agreement with values extensively reported in the literature. The age-related frequency increase is of interest and the age distribution of a patient group or control group should be taken into account in the evaluation of frequency data. The postprandial frequency-dip corresponds do the characteristics described in literature (23,31,32), when the differences in time and frequency resolution due to the several types of signal analysis are taken into account. Furthermore it should be realized that the influence of the composition of the test meal on these parameters is unknown.

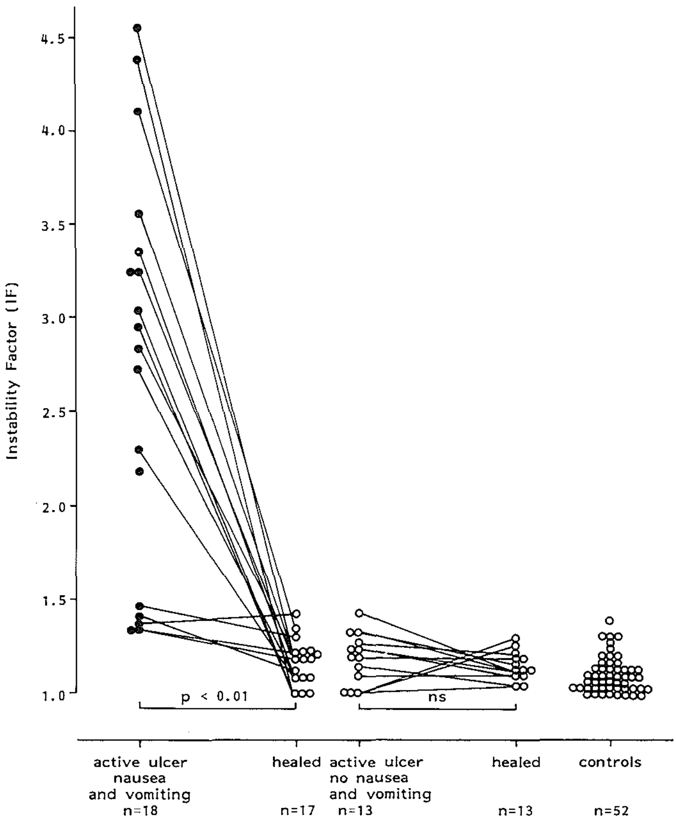


fig. 6.1.9 Graph of the postprandial instability factor (IF) in ulcer patients before and after healing, and in control subjects.

The large inter-individual difference in the amount of power increase after the test meal is probably due to the different power levels of the gastric frequency during the interdigestive state. In a previous study we demonstrated that in phase II of the interdigestive migrating complex the power of the gastric frequency in the electrogastrogramis larger, ranging from a factor 2.06 to 5.20, than during phase I (33). The recording time in the fasting state, in this study (30 min.), is short with respect to the duration of a complete cycle of the interdigestive migrating complex (125±22min) (34). Thus, the postprandial power increase would be much smaller when, during the recording in the fasting state, phase II motor activity is present than in case of motor quiescence (phase I). To obtain more precise data the fasting recording period should be extended. However, in our experience it is very difficult for a subject to lay quietly for more than 90 min., resulting in an increase of the number of motion artefacts.

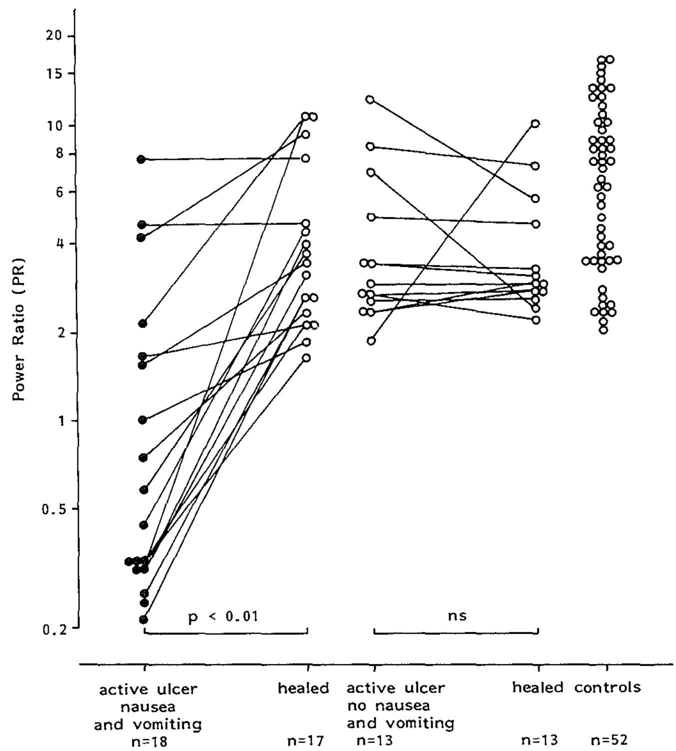


fig. 6.1.10 Graph of the power ratio (PR) in ulcer patients before and after healing, and in control subjects.

In gastric ulcer patients several types of myoelectrical abnormalities were found. One of the most interesting findings was the absence of the normal postprandial power increase, as expressed by the decrease in PR, in ulcer patients with nausea and vomiting. A possible explanation for this phenomenon and for the observed abnormal percentage of second harmonics (an indication for a waveform change in the electrogastrogram) in the fasting and postprandial state, can be found in the work of Fioramonti and Bueno (11). In their study of gastric myoelectrical activity, using serosal electrodes, in both rats and dogs with restraint-and indomethacin-induced gastric ulcerations, they reported a disorganisation of the interdigestive pattern, which consisted of continuous irregular spiking activity. This spiking activity is also known as fast oscillating potential changes superimposed on the second component, which is referred to as electrical response activity (ERA) in the current study. From previous studies (15,22) it is known that the ERA is responsible for a power increase and a change in waveform in the electrogastrogram, thus explaining the power increase and the higher percentage of second harmonics in the postprandial state observed in normal controls. If the continuous (irregular) ERA was also present in the fasting state in ulcer patients, this could explain the increased incidence of second harmonics observed in our study. There should then also have been an increase in the fasting power of the electrogastrogram which lead to a decreased PR. However, the PR is of course also determined by the power of the postprandial electrogastrogram. Fioramonti and Bueno (11) described a reduction in ERA in the postprandial state in dogs with gastric ulcerations as compared to control dogs. Electrogastrographically this reduced postprandial ERA would be reflected in a relative decrease in the postprandial power and a change in waveform when compared with normal controls. If a similar situation held true in ulcer patients this would be an additional explanation for the decreased PR observed in our study. In fact a PR below 1.00, which we frequently found, is difficult to explain by an increase of ERA in the fasting state alone, but it is explicable when a decrease in ERA in the postprandial state, is also taken into account. The significantly lower percentage of second harmonics in the postprandial phase is also in agreement with a decrease in the ERA, and thus a change in waveform, in this phase.

Bueno and Fioramonti (11) did not study the mechanical activity, so that the motor correlate of these myoelectrical abnormalities remained unclear. Recently Miranda et al (35) described the interdigestive gastric motor activity, studied manometrically, in gastric ulcer patients. They found a dramatic reduction in the occurrence of phase III in the antrum which could be in accordance with the study of Fioramonti and Bueno (11). The observed phase-II-like motor activity could be, in fact, the motor correlate of the continuous irregular ERA. Although there is no direct evidence of antral hypomotility in the postprandial phase of gastric ulcer patients, as is suggested by the decrease of ERA, gastric emptying of solids was found to be delayed, with normal emptying of liquids, which is indicative of an antral motor dysfunction (28).

The two types of frequency abnormality observed in ulcer patients with nausea and vomiting are probably due to different mechanisms. The irregular frequency variations around the normal gastric frequency suggest that the control mechanism of the gastric pacemaker is disturbed by, as yet unknown causes and that the system becomes less stable, whereas tachygastrias are thought to originate in ectopic foci (36). In view of the fact that the pacemaker region in man is thought to be situated in the oral part of the corpus along the greater curvature, and that in particular the aboral 2/3 of the stomach is electrically active (10), one would expect there to be some relationship with the location of the ulcer. It was remarkable that no significant correlation or even a trend could be established between ulcer-location and abnormal myoelectrical activity.

Another interesting question is whether a relationship was present between abnormal myoelectrical behaviour and symptoms of nausea and vomiting. There was no significant difference in the mean gastric frequency, instability factor (IF) and percentage of second harmonics during the fasting period nor in the mean gastric frequency, instability factor (IF) and percentage of harmonics during the postprandial period between the control subjects and patients with an active gastric ulcer but no symptoms of nausea and vomiting. These gastric ulcer patients did not have any tachygastrias during the fasting period either. In contrast patients with an active gastric ulcer and symptoms of nausea and vomiting had a significantly different instability factor (IF) and percentage of second harmonics during both the fasting and postprandial periods when compared with control subjects and gastric ulcer patients without nausea and vomiting. Their power ratio was also significantly different. Tachygastrias of considerable duration were observed in 4 gastric ulcer patients with nausea and vomiting. In a previous study we demonstrated that in 48 patients with "unexplained" nausea and/or vomiting, i.e. nausea and/or vomiting that cannot be accounted for by conventional diagnostic approaches, the same characteristic abnormal myoelectrical behaviour was found (37,38,39). In addition, this abnormal myoelectrical behaviour, in particular the abnormal postprandial power behaviour, was significantly correlated with a delayed gastric emptying of solids (39).

Thus, abnormal gastric myoelectrical activity in the presence of an active gastric ulcer seemed to be predominantly associated with symptoms of nausea and vomiting and was not merely due to the presence of the ulcer itself.

6.1.6 References

1. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
2. Aldrete J.S., Shepard R.B., Halpern N.B., Jiminez H., Piantadosi S. Effects of various operations on the electrical activity of the human stomach recorded during the postoperative recovery period. Ann. Surg. 1982; 195: 662-669.
3. Bortolotti M., Labo G., Serantoni C., Ciani P. Effect of highly selective vagotomy on gastric motility of duodenal ulcer patients. Digestion 1978; 17: 108-120.
4. Stoddard C.J., Smallwood R.H., Brown B.H., Duthie H.L. The immediate and delayed effects of different types of vagotomy on human gastric myoelectrical activity. Gut 1975; 16: 165-170.
5. Stoddard C.J., Smallwood R.H., Duthie H.L. Electrical arrhythmias in the human stomach. Gut 1981; 22: 705-712.
6. Kwong N.K., Brown B.H., Whitteaker G.E., Duthie H.L. Electrical activity of the gastric antrum in man. Brit. J. Surg. 1970; 57: 913-916.
7. Morton H.S. The potentialities of the electrogastrograph. Ann. R. Coll. Surg. Engl. 1954; 15: 351-373.
8. Goodman E.N., Colcher H., Katz G.M., Bangler C.L. The clinical significance of the electrogastrogram. Gastroenterology 1955; 29: 598-608.
9. Sobakin M.A., Smirnov I.P., Mislin L.N. Electrogastrography. IRE Trans. Bio. Med. Electron 1962; 9: 129-132.
10. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transsection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.
11. Fioramonti J., Bueno L. Gastrointestinal myoelectrical activity disturbances in gastric ulcer disease in rats and dogs. Dig. Dis. Sci. 1980; 25: 575-580.
12. Telander R.L., Morgan K.G., Kreulen D.L., Schmalz P.F., Kelly K.A., Szurszewski J.H. Human gastric atony with tachygastria and gastric retention. Gastroenterology 1978; 75: 497-501.
13. You C.H., Lee K.Y., Chey W.Y., Menguy R. Electrogastrographic study of patients with unexplained nausea, bloating and

vomiting. Gastroenterology 1980; 79: 311-314.
14. You C.H., Chey W.Y., Lee K.Y., Menguy R., Bortoff A. Gastric and small intestinal myoelectric dysrhythmia associated with chronic intractable nausea and vomiting. Ann. Int. Med. 1980; 95: 449-451.
15. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. What is measured in electrogastrography ? Dig. Dis. Sci. 1980; 25: 179-187.
16. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. Postprandial and interdigestive gastric electrical activity in the dog recorded by means of cutaneous electrodes. In: Gastrointestinal motility. Christensen J. (ed.) New York: Raven Press, 1980, pp187-194.
17. Brown B.H., Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.
18. Thouvenot J., Tonkovic S., Penaud J. Electrosplanchnography: method for electrophysiological exploration of the digestive tract. Acta Med. Iugosl. 1973; 27: 227-247.
19. Smallwood R.H., Brown B.H., Duthie H.L. An approach to the objective analysis of intestinal smooth muscle potentials recorded from surface electrodes. In: Proc. 5th Int. Symposium on Gastrointestinal Motility. Vantrappen G., (ed.), Leuven, Belgium, Typoff-Press, 1975, pp.248-253.
20. Abell T., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in humans shown by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.
21. Bertrand J., Dorval E.D., Metman E.H., De Calan L, Ozoux J.P. Electrogastrography and serosal electrical recording of the antrum after proximal vagotomy in man. (Abstr) Gastroenterology 1984; 86: 1026.
22. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.
23. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals

recorded from dogs and man. In: Motility of the digestive tract. Wienbeck M., (ed.), New York: Raven Press, 1982, pp.241-250.

24. Mirizzi N., Scafoglieri U. Optimal directions of the electrogastrographic signal in man. Med. Biol. Eng. Comp. 1983; 21: 385-389.

25. Smout A.J.P.M., Van der Schee E.J., Akkermans L.M.A., Grashuis J.L. Recording of gastrointestinal activity from surface electrodes. Scan. J. Gastroent. 1984; 19: suppl. 96: 11-18.

26. Geldof H., Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Electrogastrography. In: Gastric and gastroduodenal motility. Akkermans, Johnson, Read, (eds.) New York: Praeger Publishers, 1984, pp.163-175.

27. Blackman R.B., Tukey J.W. The measurement of power spectra. Dover Publications Inc, New York, 1958.

28. Hiller L.J., Malagelada J-R., Longstreth G.F., Go V.L.W. Dysfunctions of the stomach with gastric ulceration. Dig. Dis. Sci. 1980; 25: 857-864.

29. Merquelan B., Ippoliti A., Sturdevant R. Gastric emptying in patients with gastric ulcer. (Abstr). Gastroenterology 1978; 74: 1070.

30. Rhodes J., Barnardo D.E., Phillips S.F., Rovelstad R.A., Hoffman A.F. Increased reflux of bile into the stomach in patients with gastric ulcer. Gastroenterology 1969; 57: 241-252.

31. Duthie H.L., Kwong N.K., Brown B.H., Whittaker G.E. Pacesetter potential of the human gastroduodenal junction. Gut 1971; 12: 250-256.

32. Nelson T.S., Kohatsu S. Clinical electrogastrography and its relation to gastric surgery. Am. J. Surg. 1968; 116: 215-222.

33. Geldof H., Van der Schee E.J., Grashuis J.L. Electrogastrographic characteristics of interdigestive migrating complex in humans. Am. J. Physiol. 1986; 250: G165-G171.

34. Nishioka T., Sekiguchi T., Kogure M., Kusano M., Arai H., Katoh R., Okamura S., Matsuzaki T., Fukazawa T., Akiyama T., Ohwada H., Kobayashi S. A study on continuous simultaneous

recordings of gastrointestinal motility and intraluminal pH in human healthy subjects. Jpn. J. Gastroenterol. 1981; 78: 2065-2073.

35. Miranda M., Defilippe C., Valenzuela J.E. Abnormalities of interdigestive motility complex and increased duodenogastric reflux in gastric ulcer patients. Dig. Dis. Sci. 1985; 30: 16-21.

36. Gullikson G.W., Okuda H., Shimizu M., Bass P. Electrical arrhythmias in gastric antrum of the dog. Am. J. Physiol. 1980; 239: G59-G68.

37. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Electrogastrographic findings in patients with nausea and vomiting. (Abstr) Gut 1983; 24: A476.

38. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Gastric dysrhythmia; an electrogastrographic study. (Abstr) Gastroenterology 1983; 84: 1163.

39. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. An electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting. Gut, 1986; 27: 799-808.

6.2 AN ELECTROGASTROGRAPHIC STUDY OF GASTRIC MYOELECTRICAL ACTIVITY IN PATIENTS WITH UNEXPLAINED NAUSEA AND VOMITING

Published in Gut 1986; 27: 799-808.
Co-authors E.J. van der Schee, M. van Blankenstein, J.L. Grashuis.

6.2.1 Abstract

Using cutaneous electrodes an electrogastrographic study was made of gastric myoelectrical activity in both the fasting and postprandial states in 48 patients with unexplained nausea and vomiting and in 52 control subjects. A gastric emptying study, using a radio-labelled solid phase meal, was performed in 30 of these 48 patients. A follow-up study was done after 1 year. In 48% of the patients abnormal myoelectrical activity was found which was characterized by: 1) instability of the gastric pacemaker frequency; 2) tachygastrias in both the fasting and postprandial states; 3) the absence of the normal amplitude increase in the postprandial electrogastrogram. This last characteristic was correlated with a delayed gastric emptying of solids. The present study demonstrates that with electrogastrography in a heterogeneous group of patients with unexplained nausea and vomiting a subgroup can be discerned with abnormal myoelectrical activity. Our findings suggests that this abnormal myoelectrical is related with these symptoms.

6.2.2 Introduction

Patients with 'unexplained' nausea and vomiting, which are often accompanied by belching, epigastric bloating, early satiety and sometimes symptoms of the lower GI tract such as constipation and diarrhoea, constitute a heterogeneous group. Although the two main symptoms are suggestive of disturbed gastric motility, an overlap with other disorders, such as the irritable colon syndrome or rumination, cannot be excluded. Myoelectrical activity plays an important role in the control of gastrointestinal motility, therefore investigation of gastric myoelectrical activity may be helpful in identifying gastric motor disturbances (1-5).

The stomach has an inherent rhythmic myoelectrical activity with a repetition frequency of about 0.05 Hz, which is referred to as electrical control activity (ECA) (6,7). When motor activity is present, the ECA is accompanied by a second component, with or without superimposed fast oscillating potential changes, referred to as electrical response activity (ERA) (7).

The most frequent dysrhythmias described in patients with unexplained nausea and/or vomiting are the so called tachygastrias, typified by ECA frequencies 2-4 times higher than normal (1-5). The studies cited were performed using either peroral (suction) electrodes or serosal electrodes placed at laparotomy and recordings were made only in the fasting state. However, such invasive methods are not very suitable for the study and follow up of a large group of patients. An extra disadvantage of recordings with peroral suction electrodes is that it is uncertain if this method is reliable in the postprandial state.

Gastric myoelectrical activity can be recorded in a non-invasive way by means of electrodes attached to the abdominal skin. This method is known as electrogastrography (EGG) and the recorded signal as an electrogastrogram. EGG allows the recording of gastric myoelectrical activity in both the fasting and postprandial states, providing information about the gastric ECA frequency, ERA and tachygastrias (8-16).

In the present study gastric myoelectrical behaviour was recorded by EGG in both the fasting and postprandial states in patients with prolonged, unexplained nausea and vomiting. Gastric emptying of solids was also measured to determine whether abnormal myoelectrical behaviour was associated with a delay in this gastric emptying. A follow-up study was done after about 1 year.

6.2.3 Materials and methods

Subjects. Forty-eight patients (17 men and 31 women, mean age 42 years, range 8 - 71) participated in the study. All 48 patients complained of frequent (more than 3 times a week) nausea and vomiting, accompanied by one or more of the following symptoms: belching, abdominal distension, sense of fullness after a normal meal and inability to finish a normal meal. The symptoms, for which no organic cause had been found, had lasted for at least 3 months (median 9 months, range 3 - 62). The diagnostic work-up included a clinical evaluation, appropriate laboratory tests, ultrasound scanning of the upper abdomen, and upper gastrointestinal endoscopy. Thirty of the 48 patients consented to a gastric emptying study using a radio-labelled solid-phase meal as described in detail by Akkermans et al (17) and Jacobs et al (18,19). Gastric emptying was considered to be delayed if the percentage emptied in 1 hr was more than two standard deviations below the mean of control subjects (19). Exclusion criteria were a history of systemic illness (e.g. diabetes mellitus, rheumatic disorders or vasculitus), neurological or psychiatric disorders, or previous gastrointestinal or biliary surgery. Patients taking any drug were excluded, with the exception of those taking gastrointestinal prokinetic drugs such as metoclopramide or domperidone, which were stopped at least 1 week before the EGG and gastric emptying study.

In 36 patients a follow-up study after about 1 year (range 11 - 13 months) was possible. The gastric emptying study was repeated in those patients in whom this had initially been carried out (20 patients).

Control subjects were 27 men and 25 women (mean age 42, range 16 - 75) without any history of gastrointestinal or systemic disorder.

The study was approved by the Medical Ethics committee of the Erasmus University, Rotterdam, on June 4, 1982 and carried out with the informed consent of the subjects.

Technique of recording. Although in most subjects an optimal electrode direction coincides with the antral axis (20), the optimum electrode position cannot be defined exactly because of inter-individual anatomical variations (21,22).

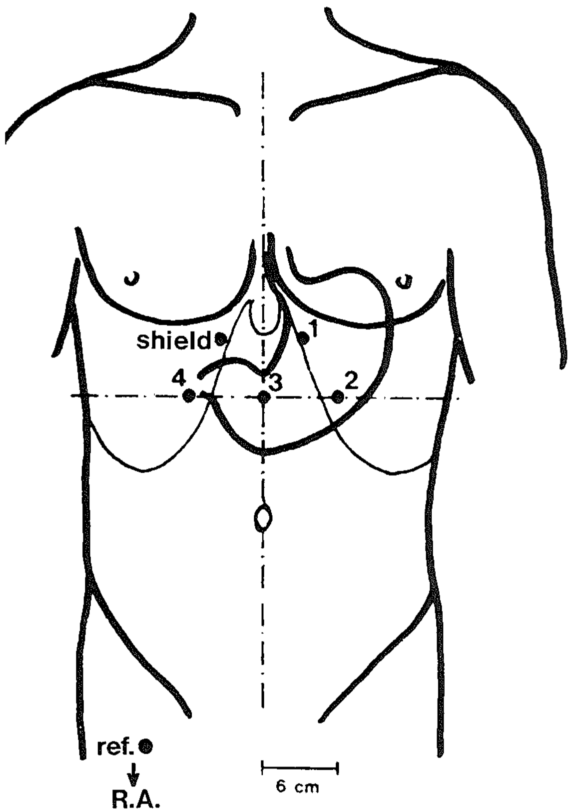


fig. 6.2.1 Electrode positions used in this study. Electrodes 2,3 and 4 are situated on a transverse line halfway between the lower end of the sternum and the umbilicus. Electrode 3 is placed at the intersection of this line and the median plane. Distance between all abdominal electrodes is 6 cm. Reference electrode is on the right ankle (RA). The shield electrode was used to reduce possible interference from the 50 Hz mains voltage at the input stage of the preamplifiers.

Therefore several leads were used and the signal with the best signal to noise ratio was then selected for further analysis. In this choice contamination of the signal with a respiration component is of less importance than are large motion artefacts, which occur in particular in the monopolar leads. The positions of the 6 recessed-type electrodes (Red Dot 2256, 3M Co.) used in this study are shown in fig. 6.2.1. A strain gauge respiration transducer was attached to the thoracic wall. Activity during fasting was recorded for a 30 min period after an overnight fast. A test meal consisting of 250 ml of yoghurt with 20 g of sugar was then given, and consumed within 4 min, while the recording was continued. The composition of the test meal was: 990 kJ, 8.75 g protein, 8.75 g fat and 30 g carbohydrate. The recording was stopped 35 min after the start of the test meal. Subjects lay quietly in a supine position during most of the recording session (only sitting up while taking the test meal). The 4 monopolar and 6 bipolar signals were recorded on paper (Van Gogh EP-8b) and simultaneously stored on magnetic tape (Racall Store 14). The high- and low-pass filters (6 decibel/octave) were set at 0.01 and 0.5 Hz respectively (21).

Signal analysis. A fast Fourier transform algorithm implemented on a NOVA 2 digital computer was used to obtain power spectra of the time signals. The signals, replayed from tape 16 times faster than real time, were preprocessed by band-pass filtering using a butterworth filter (24 decibel/octave) with (real time) cut-off frequencies set at 0.01 and 0.5 Hz, to remove possible DC components and to avoid aliasing. They were then digitized (real time sampling frequency 1 Hz) and fed into the computer. The time signal of the whole recording period was used for signal analysis. Spectra were obtained as follows: every 64 s a power spectrum was computed from the preceeding 256 s of the EGG time-signal, to which a Hamming window had been applied to reduce leakage (23). These time values have been shown to enable the extraction of relevant information from the EGG, giving 129 points per spectrum and a frequency spacing of 0.0039 Hz (16). Tachygastrias which have a duration of at least 64 s can be detected using these time values

(16). This procedure generate a series of overlapping spectra, called running spectra. They were plotted in two different ways, using pseudo-3-dimensional and grey-scale plots. The grey-scale plot, in particular, enables the easy recognition of frequency patterns. Relative power changes can be recognized more precisely in the pseudo-3-dimensional plot. Plots were made on a Versatec 1100 A printer plotter. The mean gastric frequency (Hz) with standard deviation (SD) and its power content were computed for both the fasting and postprandial states. An Instability Factor (IF) was calculated to give a measure of the variability in the ECA frequency visible in grey-scale plots. This was defined as the ratio of the frequency SD of the whole fasting or postprandial period to the frequency SD of one, arbitrary choosen, spectrum containing a clearly present gastric frequency component in the fasting or postprandial state respectively.

Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance to the stomach wall) it is impossible to make a comparison of inter-individual and even intra-individual power data. Therefore in this study only power changes in one single recording session were used for analysis. To quantify the postprandial power change,the ratio of the power in the postprandial state to the power in the fasting state was computed and referred to as the Power Ratio (PR).

Where it was considered to be necessary running spectrum analysis of the respiration signal was performed to exclude confusion between frequencies of respiratory origin and possible tachygastrias.

The only parameter associated with the electrogastrographic waveform that was used in this study was the presence of a second harmonic in the spectrum. Higher harmonics can be recognized in the spectrum because their frequency spacing forms exactly an integer. The more a periodic signal deviates from a sinusoid, the more harmonics may be expected to be present. A second harmonic of the gastric frequency was considered to be present if its power amounted to at least 5% of the power of the first harmonic, i.e.

the gastric frequency itself.

Statistical analysis. Dichotomized data were compared using Fisher's exact test. To compare continuous data between groups the Mann-Whitney U-test (non-parametric) was used. Regression lines (least square method) and coefficients of correlation (r) were calculated for normally distributed data, otherwise the Spearman rank correlation coefficient was calculated. Probability (p) values were derived from two-tailed tests with 0.05 being taken as the significant level.

6.2.4 Results

A total of 136 standard recordings were made in 100 subjects. In the control group 3.1% of the total recording time (the initial 2-3 spectra after food intake) could not be interpreted because of motion artefacts during food intake. In the patient group 4.7% of the recording time was lost as the result of artefacts caused by food intake and vomiting.

Control Group. The results in the control group are summarized in table 6.2.1. In the fasting state a gastric ECA frequency of relatively low power was found with negligible frequency variations, as was indicated by an Instability Factor (IF) close to 1. Immediately after the test meal a frequency dip was observed in every subject. The average frequency decrease was 23% of the fasting frequency. After about 5 min the frequency started to increase again, generally resulting in a temporary overshoot (fig. 6.2.2). After that the frequency, referred to as the postprandial frequency, stabilized at a level which was at least equal to or somewhat higher than the fasting frequency. The range of the postprandial IF, which was the same as in the fasting state, confirmed the impression obtained by visual inspection of the grey-scale plots that the postprandial frequency was also stable. Although the power of the gastric frequency increased by at least a factor 2 after the test meal, the range of the Power Ratio (PR) indicated large inter-individual differences. A second harmonic was more often observed in the postprandial than in the fasting state. Tachygastrias were not seen in the control group. The frequency and power pattern shown in fig. 6.2.2 was representative for this group.

Table 6.2.1. EGG parameters in the control group and in patients with unexplained nausea and vomiting. The division of the patients into subgroups was based on the normal ranges found in the control group. If the postprandial IF or PR exceeded the normal range the EGG was considered abnormal. Tachygastrias were also considered abnormal.

	Control group	Patient Group n=48	
		normal EGG	abnormal EGG
	n=52	n=25	n=23
Age (yrs)	36	39	47
	16–75	18–71	8–66
Duration complaints (mo)		10	12
		3–62	3–60
Fasting state			
Frequency (Hz)	0.050	0.049	0.051
	0.045–0.055	0.045–0.055	0.045–0.059
Instability factor (IF)	1.12	1.14	1.20
	1.00–1.40	1.00–1.39	1.00–3.10
Second harmonic	38.5	44	60.9
Tachygastrias	0	0	6
Postprandial state			
Frequency (Hz)	0.054	0.052	0.051
	0.047–0.064	0.047–0.058	0.042–0.060
Instability factor (IF)	1.10	1.10	2.05
	1.00–1.40	1.00–1.37	1.00–4.00
Second harmonic	67.3	72	17.4*
Power ratio (PR)	6.79	4.13	0.87
	2.08–16.61	2.09–16.01	0.17–15.06
Tachygastrias	0	0	3

The results are expressed as median and range with the exception of the second harmonic (%) and tachygastrias (number of patients).
p-value for the difference between the groups: * $p = 0.0002$.

Both the fasting and postprandial ECA frequencies increased with age (fasting: r = 0.78, p = 0.00005, regression line: fasting frequency(mHz) = 0.13 x age(yr) + 44.316; postprandial: r = 0.71, p = 0.00005, regression line: postprandial frequency(mHz) = 0.20 x age(yr) + 46.213). The remaining EGG parameters were not influenced by age, nor was there any correlation between sex and any EGG parameter.

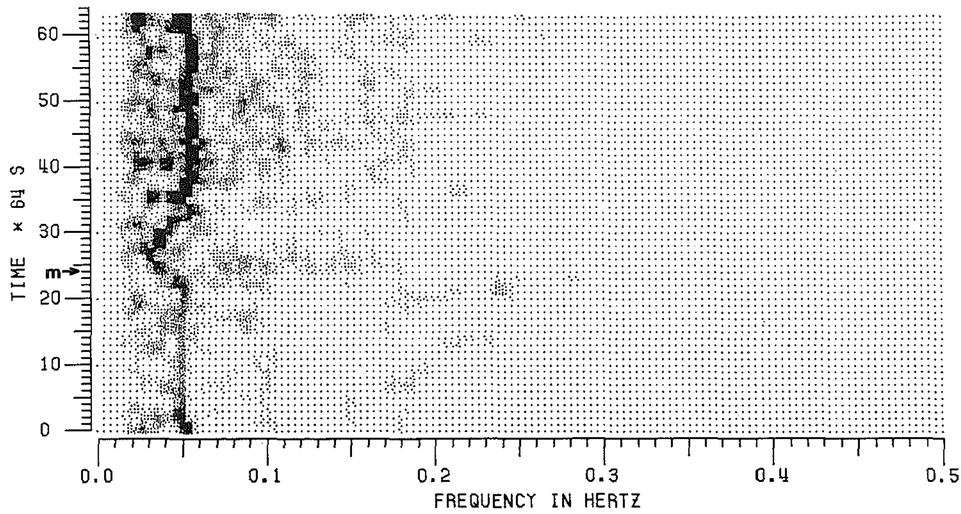


fig. 6.2.2 Grey-scale plot of the electrogastrogram of a control subject. The blackness is proportional to the magnitude of power of the EGG signal, divided into 36 distinct grey levels. Note the frequency dip following the test meal marked with "M".

Patient Group. The results of the EGG parameters are summarized in tables 6.2.1, 6.2.2 and 6.2.3. Several types of abnormal myoelectrical activity were observed in this group.

An unstable gastric ECA frequency was seen in the grey-scale plots of some patients. Although small variations in the gastric ECA frequency were observed in the control group (fig. 6.2.2), the frequency variations observed in these patients were much more pronounced, as is illustrated in fig. 6.2.3. These frequency variations were mainly seen in the postprandial state and were accompanied by an unstable fasting frequency in only a minority of the patients. Normally the postprandial frequency is equal or somewhat higher than the fasting frequency, but in these patients it repeatedly jumped abruptly to another, mostly lower, value (fig. 6.2.3). The instability factor (IF) quantifies these frequency variations. In 25% of the patients an IF was found falling far beyond the range of the IF in the control group.

Table 6.2.2. EGG parameters in patients with unexplained nausea and vomiting. Normal versus delayed gastric emptying for a solid-phase meal.

	Patients with normal gastric emptying n=17	Patients with delayed gastric emptying n = 13
Age (yrs)	40	42
	19–65	8–61
Duration complaints (mo)	12	18
	4–62	3–60
Fasting state		
Frequency (Hz)	0.050	0.050
	0.045–0.059	0.047–0.054
Instability factor (IF)	1.22	1.28
	1.00–1.67	1.00–1.76
Second harmonic	52.9	53.8
Tachygastrias	3	2
Postprandial state		
Frequency (Hz)	0.052	0.051
	0.042–0.058	0.043–0.058
Instability factor (IF)	1.25	1.33
	1.00–2.52	1.00–4.00
Second harmonic	64.7	7.7*
Power ratio (PR)	4.13	0.85**
	2.09–15.06	0.20–1.99
Tachygastrias	0	2

The results are expressed as median and range with the exception of the second harmonic (%) and tachygastrias (number of patients).
p-value for the difference between the groups: * p = 0.002, ** p = 0.0001.

Tachygastrias were observed in 8 patients, in 5 cases it only occurred in the fasting state, in 2 only in the postprandial state, and in 1 patient in both the fasting and postprandial states (fig. 6.2.4 and 6.2.5). Tachygastrias lasted between 3 and 14 minutes.

Another interesting finding was the absence of the normal postprandial power increase (PR<1) in 33% of the patients. In these patients either no power change or a postprandial power decrease was observed (fig. 6.2.6).

In all patients a frequency dip was observed identical to that found in the control group.

Table 6.2.3. EGG parameters in patients with unexplained nausea and vomiting after a follow-up period of 1 year.

	Patients without complaints n=12	Patients with persisting complaints n=24
Age (yrs)	41	39
	24–66	19–72
Duration complaints (mo)	16	42
	11–61	,16–72
Fasting state		
Frequency (Hz)	0.050	0.049
	0.046–0.055	0.043–0.054
Instability factor (IF)	1.17	1.41*
	1.00–1.35	1.00–2.83
Second harmonic	33.3	45.8
Tachygastrias	0	6
Postprandial state		
Frequency (Hz)	0.054	0.052
	0.048–0.059	0.046–0.055
Instability factor (IF)	1.14	1.23*
	1.00–1.33	1.05–2.30
Second harmonic	66.2	50
Power ratio (PR)	3.55	3.07*
	2.41–15.01	0.62–12.32
Tachygastrias	0	3

The results are expressed as median and range with the exception of the second harmonic (%) and tachygastrias (number of patients).
p-value for the difference between the groups: * p = 0.005.

The patient group could be divided into 2 subgroups . Defining the ranges found in the control group for the postprandial IF and the PR as normal, and considering tachygastrias as abnormal, a subgroup of 25 patients could be split off in which all EGG parameters were identical to the control group (table 6.2.1). Even the percentage of second harmonics had the same order of magnitude as in the control group.

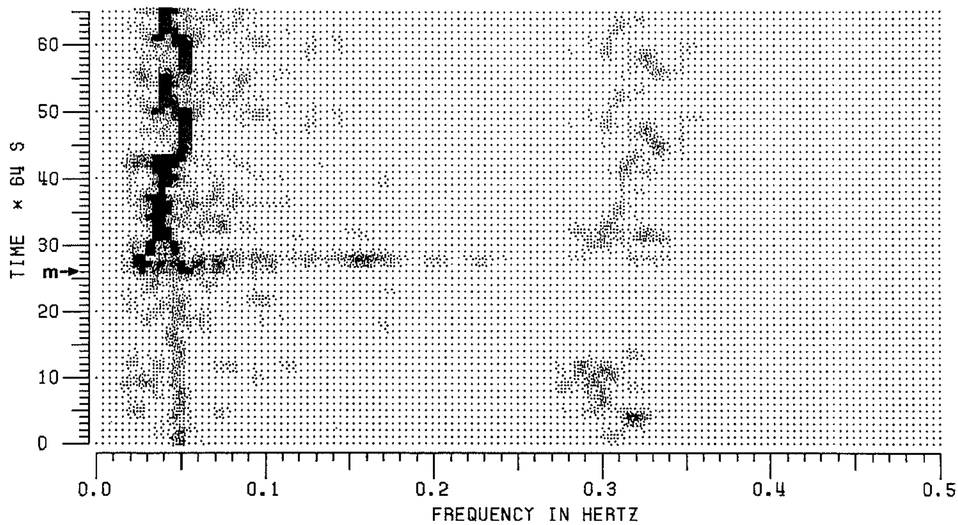


fig. 6.2.3 Grey-scale plot of an EGG demonstrating wide frequency variations in the postprandial state (IF=3.10). The frequencies at about 0.30 Hz are of respiratory origin. "M" indicates the start of the test meal.

In the remaining group of 23 patients with an abnormal electrogastrogram the enlarged range of the IF in the fasting state can be explained by the finding that in some patients besides the postprandial, the fasting ECA frequency was unstable also. It is remarkable that in this group a significant lower pecentage of second harmonics was observed in the postprandial state while in the fasting state this percentage tended to be higher.

The results from the 30 patients in whom a gastric emptying study was performed are summarized in table 6.2.2. Delayed gastric emptying for solids was observed in 13 patients, who all displayed an abnormal electrogastrogram (postprandial IF and/or PR falling beyond the range of the control group and/or the presence of tachygastrias). There was a significant difference in the PR between patients with normal and those with delayed gastric emptying for a solid-phase meal. In the subgroup with normal gastric emptying the range of the PR was almost identical to the control group. With the exception of 1 patient (PR=1.99) in whom tachygastrias were observed in both the fasting and postprandial states, all patients with delayed gastric emptying showed a power decrease after the test meal (PR < 1.00) (fig. 6.2.7).

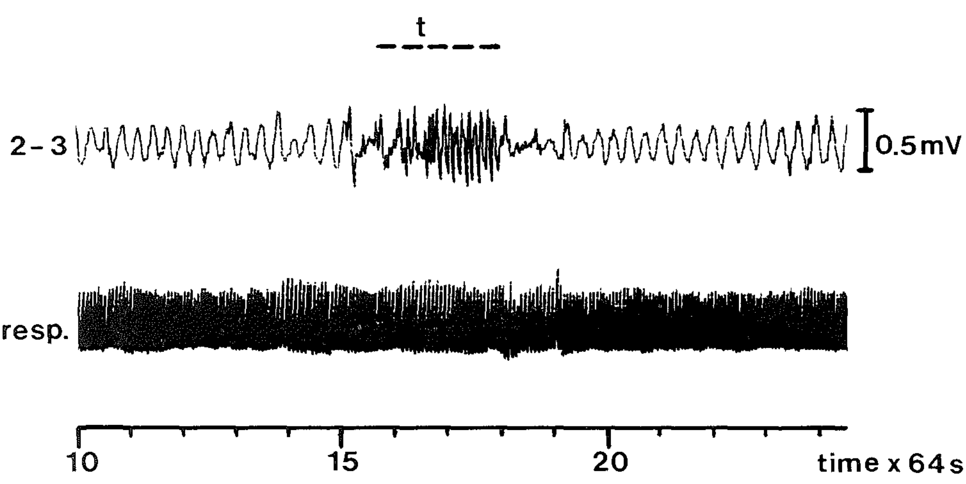


fig. 6.2.4 Part of the bipolar time signal in the fasting state from the patient with tachygastrias both in fasting and postprandial state. The tachygastria is marked by the dashed line. Bottom trace is the respiration signal.

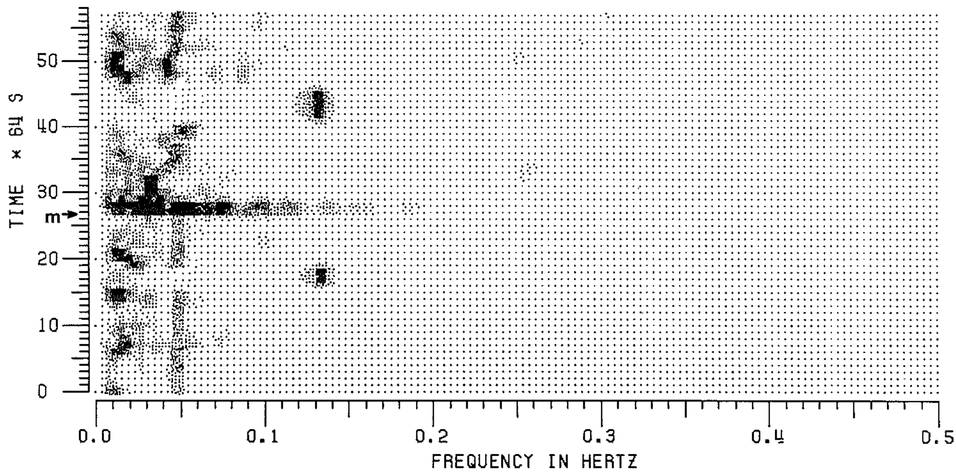


fig 6.2.5 Grey-scale plot of an EGG from the patient with tachygastrias both in fasting and postprandial states at about 0.13 Hz. Coinciding with food intake (start marked with "M") the effect of a motion artefact is visible in the spectrum. Part of the time signal in the fasting state is shown in fig. 6.2.4.

It should also be mentioned that in the patient with the prolonged tachygastria in the postprandial phase the PR was less than 1. However, not too much attention should be paid to this finding due to the short period of normal postprandial frequency available for analysis (tachygastrias not being used for the calculation of PR and IF). The abnormally low percentage of higher harmonics observed in the postprandial state in the patients with a delayed gastric emptying should be noted.

After a follow-up period of about 1 year 36 of the original 48 patients could be re-examined. The results of the follow-up study are summarized in table 6.2.3. Twelve patients were free of complaints without treatment. In 7 of these 12 the original electrogastrogram showed an unstable gastric ECA frequency (IF>2) and/or an absence of the postprandial power increase (PR<1).

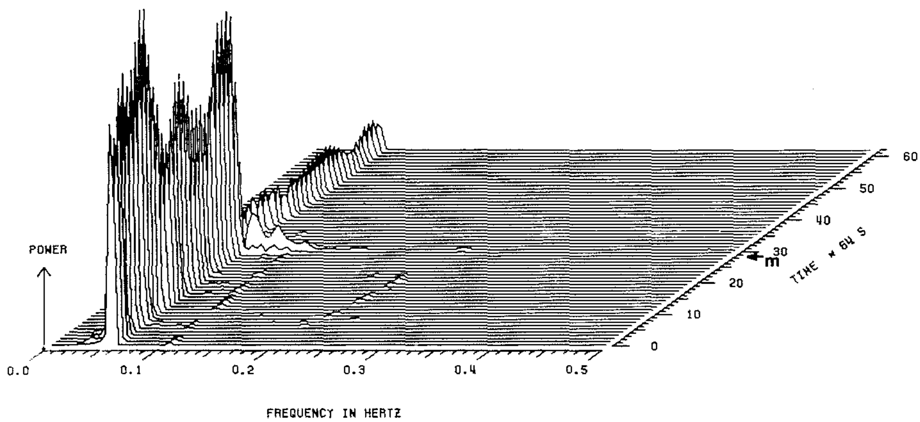


fig. 6.2.6 Pseudo-3-D display of an EGG from a patient with a postprandial power decrease (PR=0.20). Note the second harmonic visible at about 0.1 Hz in the fasting state. "M" indicates the start of the test meal.

These initially abnormal EGG parameters in these 7 patients had returned to values within the range of the control group (in fig. 6.2.7 illustrated for the PR). In the remaining 24 patients symptoms were still present, although practically all had benefited to a greater or lesser degree from treatment with prokinetic drugs such as metoclopramide and domperidone in combination with dietary advice. The EGG parameters in the 24 patients with persisting complaints were similar to those found in the original recording (in fig. 6.2.7 illustrated for the PR). The 8 patients in whom tachygastrias had been observed initially still had tachygastrias, although the duration (range 4-9 minutes) varied per patient. No abnormalities were found in the frequency dip in the follow-up study.

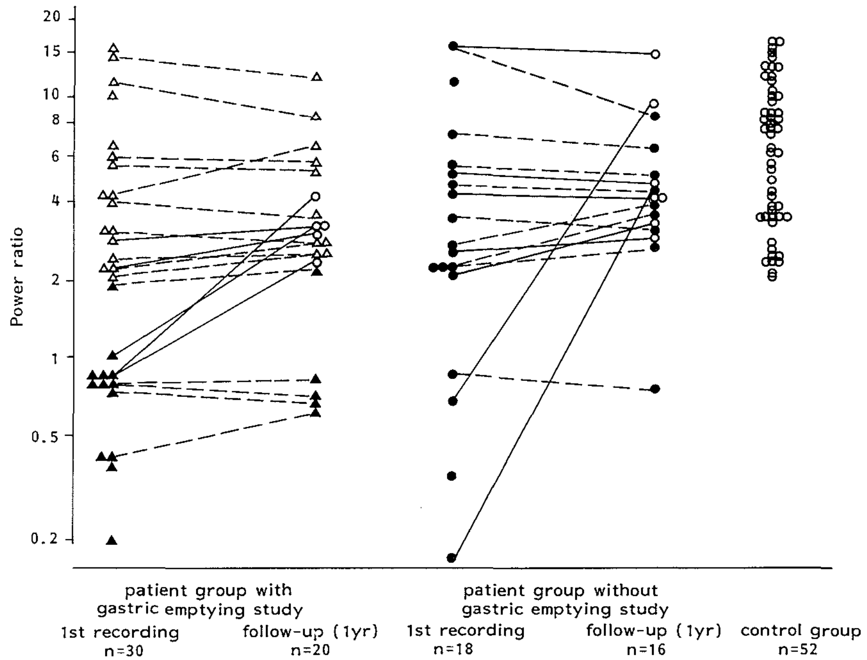


fig. 6.2.7 Graph of the course of the power ratio (PR) in patients with unexplained nausea and vomiting. △ : patient with nausea and vomiting and normal gastric emptying; ▲ : patient with nausea and vomiting and delayed gastric emptying; ● : patient with nausea and vomiting; no gastric emptying study; ○ : patient in remission (and normal gastric emptying when this study was performed). Continuous lines in case of remission. Dotted line with persisting complaints.

A repeat gastric emptying study was performed in 20 patients of whom 5 had experienced a symptomatic remission. In 3 of these 5 patients the initial gastric emptying was delayed and had returned to normal after 1 year. The initial abnormal PR (PR<1) in these 3 patients returned to normal as is illustrated in fig. 6.2.7. In the remaining 15 patients with persisting complaints no essential changes were found in the emptying rate, PR (fig. 6.2.7) and IF.

6.2.5 Discussion

The values for the fasting and postprandial gastric ECA frequencies in the control group correspond with values reported in the literature (6,8,16). The increase in the fasting and postprandial ECA frequencies with age, observed in this study, probably explains the small differences found between the referred studies. Since the mechanism and the motor correlate of the postprandial frequency dip are still unknown and the quantity and composition of the test meal may well influence the timing and frequency values of the dip, care should be taken in comparing data concerning the postprandial frequency dip. Nevertheless results from the present study are in general agreement with the literature (16,24,25).

In the patient group 48% of the subjects with complaints suggestive of gastric motility disorders displayed characteristic abnormalities in gastric myoelectrical behaviour. Both frequency and power abnormalities were observed in the fasting and postprandial states. The recorded frequency abnormalities can be divided into 1) frequency variations around the normal gastric ECA frequency at about 0.05 Hz (fig. 6.2.3), suggestive of a disturbed control mechanism of the gastric pacemaker, and 2) tachygastrias. Tachygastrias, a term introduced by Code and Marlett (26), are thought to be generated in an antral ectopic focus which overrides the normal gastric pacemaker. Tachygastrias were seen in 8 out of 48 patients. This incidence is less than reported by You et al (2), and Chey et al (5), who found tachygastrias in 9 out of 14 and 35 out of 70 patients respectively. However, it is not known to what extent the mucosal suction electrodes, used in these studies, may have given rise to tachygastrias. It should also be realized with regard to the present study that EGG has its limitations in the detection of tachygastrias shorter than 64 s (16). Although tachygastrias in the fasting state have been reported in the absence of any gastric symptoms (27), it is generally assumed that no motor activity is present during a tachygastria (1-5,28). This view is not in conflict with the fact that in the 2 patients with a postprandial tachygastria a delayed gastric emptying was observed.

The characteristic abnormality observed in the power pattern in patients was an absence of the normal postprandial power increase, or even a power decrease, after the test meal. The normal postprandial power increase in the EGG signal is ascribed to the presence of ERA during motor activity (11,15). In addition ERA is responsible for a change in the waveform of the electrogastrogram (15) which explains the increased occurrence of second harmonics in the postprandial state in control subjects. Absent or diminished postprandial motor activity and thus absent or diminished ERA could be responsible for the absence of the normal postprandial power increase and the less frequent occurrence of the second harmonic in the postprandial state (table 6.2.1 and 6.2.2). Studies of gastric physiology (29-32) have led to the concept that grinding and emptying of solids are primarily a function of the gastric antrum and that the rate of gastric emptying of solids is proportional to the antral phasic pressure activity generated by the meal (33). As it is antral myoelectrical activity in particular that is recorded using EGG (15,20), the observed correlation of power abnormalities with a delayed gastric emptying of solids, i.e. antral hypomotility, leads us to the belief that the absence of the postprandial power increase indeed reflects a decreased postprandial ERA.

This study demonstrates that with electrogastrography in patients with unexplained nausea and vomiting abnormal myoelectrical behaviour can be discerned. In patients with an initial abnormal electrogastrogram (IF>2 and/or PR<1), who experienced a remission of symptoms after one year, this abnormal myoelectrical behaviour had returned to normal, while in patients with persisting symptoms the myoelectrical activity remained unchanged. In a pilot study in gastric ulcer patients (22,34,35) these same characteristic myoelectrical abnormalities were only observed in ulcer patients with nausea and vomiting. These findings suggest that EGG measurements in a heterogeneous group of patients with unexplained nausea and vomiting enable the identification of a subgroup in which abnormal myoelectrical activity is related to or even the cause of these symptoms. The observed correlation of delayed gastric emptying for solids with absence of the normal postprandial power increase, both indicative of impaired antral motor activity, supports this view. The fact that the majority of the myoelectrical abnormalities occurred postprandially underlines the importance of studying the myoelectrical activity in both the fasting and postprandial states.

6.2.6 References

1. Telander R.L., Morgan K.G., Kreulen D.L., Schmalz P.F., Kelly K.A., Szurszewski J.H. Human gastric atony with tachygastria and gastric retention. Gastroenterology 1978; 75: 497-501.
2. You C.H., Lee K.Y., Chey W.Y., Menguy R. Electrogastrographic study of patients with unexplained nausea, bloating and vomiting. Gastroenterology 1980; 79: 311-314.
3. You C.H., Chey W.Y., Lee K.Y., Menguy R., Bortoff A. Gastric and small intestinal myoelectric dysrhythmia associated with chronic intractable nausea and vomiting. Ann. Int. Med. 1981; 95: 449-451.
4. Reynolds R.P.E., Bardakjian B.L., Diamant N.E. A case of antral tachygastria: symptomatic and myoelectric improvement with gastroenterostomy and domperidone therapy. Can. Med. Assoc. J. 1983; 128: 826-829.
5. Chey W.Y., You C.H., Lee K.Y., and Menguy R. Gastric dysrhythmia: clinical aspects. In: Chey W.Y., ed. Functional disorders of the digestive tract. New York: Raven Press, 1983: 175-181.
6. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transsection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.
7. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
8. Brown B.H.,Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.
9. Thouvenot J., Tonkovic S., Penaud J. Electrosplanchnography: Method for electrophysiological exploration of the digestive tract. Acta Med. Jugosl. 1973; 27: 227-247.
10. Smallwood R.H., Brown B.H., Duthie H.L. An approach to the objective analysis of intestinal smooth muscle potentials recorded from surface electrodes. In: Vantrappen G., ed. Proc. 5th Int. Symposium on Gastrointestinal Motility, Leuven. Belgium. Typoff-Press, 1975: 248-253.
11. Smout A.J.P.M., van der Schee E.J., Grashuis J.L. What is

measured in electrogastrography? Dig. Dis. Sci. 1980; 25: 179-187.

12. Smout A.J.P.M., van der Schee E.J., Grashuis J.L. Postprandial and interdigestive gastric electrical activity in the dog recorded by means of cutaneous electrodes. In: Christensen J., ed. Gastrointestinal motility. New York: Raven Press, 1980: 187-194.

13. Abell T., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in humans shown by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.

14. Bertrand J., Dorval E.D., Metman E.H., De Calan L., Ozour J.P. Electrogastrography and serosal electrical recording of the antrum after proximal vagotomy in man. (abstr) Gastroenterology 1984; 86: 1026.

15. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.

16. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals recorded from dogs and man. In: Wienbeck M., ed. Motility of the digestive tract. New York: Raven Press, 1982: 241-250.

17. Akkermans L.M.A., Jacobs F., Oei Hong You, Roelofs J.M.M., Wittebol P. A non-invasive method to quantify antral contractile activity in man and dog (a preliminary report). In Christensen J., ed. Gastrointestinal motility. New York: Raven Press, 1980: 195-202.

18. Jacobs F., Akkermans L.M.A., Oei Hong You, Hoekstra A., Wittebol P. Effects of domperidone on gastric emptying of semi-solid and solid-food. In: Towse G., ed. Progress with domperidone, a gastrokinetic and anti-emetic agent. London: Academic press, 1981: 11-20.

19. Jacobs F., Akkermans L.M.A., Oei Hong You, Hoekstra A., Wittebol P. A radioisotope method to quantify the function of fundus, antrum and their contractile activity in gastric emptying of a semi-solid and solid-meal. In: Wienbeck M., ed. Motility of the digestive tract. New York: Raven Press,

1982: 233-240.

20. Mirizzi N., Scafoglieri U. Optimal directions of the electrogastrographic signal in man. Med. Biol. Eng. Comp. 1983; 21: 385-389.

21. Smout A.J.P.M., Van der Schee E.J., Akkermans L.M.A., Grashuis J.L. Recording of gastrointestinal activity from surface electrodes. Scan. J. of Gastroenterol. 1984; 19: suppl. 96: 11-18.

22. Geldof H., van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Electrogastrography. In Akkermans L.M.A., Johnson A.G., Read N.W. eds. Gastric and gastroduodenal motility. New York: Praeger Publishers, 1984: 163-175.

23. Blackman R.B., Tuckey J.W. The measurement of power spectra. Dover Publications Inc. New York, 1958.

24. Duthie H.L., Kwong N.K., Brown B.H., Whittaker G.E. Pacesetter potential of the human gastroduodenal junction. Gut 1971; 12: 250-256.

25. Nelson T.S., Kohatsu S. Clinical electrogastrography and its relation to gastric surgery. Am. J. Surg. 1968; 116: 215-222.

26. Code C.F., Marlett J.A. Canine tachygastria. Mayo Clin. Proc. 1974; 49: 325-332.

27. Stoddard C.J., Smallwood R.H., Duthie H.L. Electrical arrhythmias in the human stomach. Gut 1981; 22: 705-712.

28. You C.H., Chey W.Y. Study of electromechanical activity of the stomach in humans and dogs with particular attention to tachygastria. Gastroenterology 1984; 86: 1460-1468.

29. Dozois R.R., Kelly K.A., Code C.F. Effect of distal antrectomy on gastric emptying of liquids and solids. Gastroenterology 1971; 61: 675-681.

30. Mroz C.T., Kelly K.A. The role of the extrinsic antral nerves in the regulation of gastric emptying. Surg. Gynecol. Obstet. 1977; 145: 369-377.

31. Hinder R.A., Kelly K.A. Canine gastric emptying of solids and liquids. Am. J. Physiol. 1977; 233: E335-E340.

32. Rees W.D.W., Miller L.J., Malagelada J-R. Dyspepsia, antral motor dysfunction, and gastric stasis of solids. Gastroenterology 1980; 78: 360-365.

33. Camilleri M., Brown M.L., Becker G., Zinsmeister A.R., Malagelada J-R. Relationship between antral pressure activity and gastric emptying in man. (abstr) Dig. Dis. Sci. 1984; 29: 564.
34. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Electrogastrographic findings in patients with nausea and vomiting. (Abstr) Gut 1983; 24: A476.
35. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Gastric dysrhythmia; an electrogastrographic study. (Abstr) Gastroenterology 1983; 84: 1163.

6.3 EFFECTS OF HIGHLY SELECTIVE VAGOTOMY ON GASTRIC MYOELECTRICAL ACTIVITY; AN ELECTROGASTROGRAPHIC STUDY

Submitted for publication.

Co-authors E.J. van der Schee, M. van Blankenstein, D.L. Westbroek.

6.3.1 Abstract

Changes in gastric myoelectrical activity following highly selective vagotomy were studied in 12 patients by means of electrogastrography (EGG) using cutaneous electrodes. Measurements were made before, 10 days after and 6 months after operation. Eight patients undergoing cholecystectomy served as controls. Preoperatively all controls and patients had normal recordings. In the cholecystectomized patients no significant changes were found postoperatively. Ten days after highly selective vagotomy the normal initial postprandial dip in gastric ECA frequency and the subsequent increase in frequency and power were not seen. Tachygastrias were observed in 3 patients. Six months after operation the normal frequency and power responses to a test meal had returned, but both the fasting and postprandial ECA frequencies were significantly raised. It can be concluded that highly selective vagotomy is associated with changes in the myoelectrical behaviour, in particular in the postprandial state, which are partly reversible with time. The changes in the postprandial power response in patients after highly selective vagotomy could possibly reflect a temporary failure to convert the interdigestive motility pattern into a feeding pattern.

6.3.2 Introduction

Highly selective vagotomy (HSV), also known as proximal gastric vagotomy, has been advocated as an acid-reducing operation for the treatment of peptic ulcer patients who do not respond adequately to medical treatment. Although highly selective vagotomy was developed to reduce the motility problems that occur after truncal vagotomy it, too, leads to motility disorders (1-6).

Myoelectrical activity plays an important role in the control of gastric motor activity. The effects of vagotomy on gastric myoelectrical activity are therefore of potential interest with regard to the study of gastric motility following vagotomy. The stomach has an inherent rhythmic myoelectrical activity with a repetition frequency of about 0.05 Hz, referred to as slow waves or, as in this study, electrical control activity (ECA) (7,8). When motor activity is present, the ECA is accompanied by a second component referred to in this study as electrical response activity (ERA). The ERA may or may not display superimposed fast oscillating potential changes (also called spikes or spike activity) (8).

Several groups have investigated the effects of vagotomy on the myoelectrical behaviour of the stomach and have found changes, which include tachygastrias and changes in gastric ECA frequency (1-3,5,9). In addition changes have been found in the amplitude and waveform of the gastric ECA following vagotomy (2). However, discrepancies exist between the results reported by the various groups, which could be due to differences in timing of the recording in the postoperative period, differences in the extent of the vagotomy or to differences in the recording or signal analysis methods used. Most of these studies were performed using either peroral (suction) electrodes or serosal electrodes placed at laparotomy and, in general, recordings were only made in the fasting state.

With the development of electrogastrography (EGG) using skin electrodes it has become possible to examine gastric myoelectrical activity in a non-invasive fashion in both the fasting and postprandial states, thus providing information about the gastric ECA frequency, the presence of ERA and tachygastrias (10-19).

Because of our interest in electrogastrographic abnormalities in various disease states (20-22), we studied patients undergoing highly selective vagotomy before operation, shortly after operation following return to an unrestricted diet, and 6 months later, to detect both early and late changes in myoelectrical behaviour.

6.3.3 Methods

Subjects. Twelve patients (7 men and 5 women, mean age 49, range 27 - 60) participated in the study. In all patients a proximal gastric vagotomy was performed for duodenal ulceration. None had a history of any other gastrointestinal or systemic disorder. Up to the day of operation the patients were treated with a histamine 2-receptor antagonist. Highly selective vagotomy was performed using accepted techniques (23). Reduction in gastric acid output after stimulation by insulin-induced hypoglycaemia was used to test if the vagotomy was complete.

The control subjects were 3 men and 5 women (mean age 52, range 34 - 68) undergoing a cholecystectomy, but with no history of any other gastrointestinal or systemic disorder.

Recording technique. Gastric myoelectrical activity during the fasting and postprandial states was recorded in all subjects the day before operation, 10 days after operation and 6 months after operation.

Although in most subjects the optimal electrode direction coincides with the antral axis (24), the optimum electrode position cannot be defined exactly because of inter-individual anatomical variations (20,25). Therefore several leads were used and the signal with the best signal to noise ratio was then selected for further analysis. In this selection contamination of the signal by a respiration component is of less importance than are large motion artefacts, which occurred particularly in the monopolar leads, because the signal analysis technique used in this study separates respiration frequencies from gastric frequencies (15,22). The positions of the 6 recessed-type electrodes (Red Dot 2256, 3M Co.) used in this study are shown in fig. 6.3.1. A strain gauge respiration transducer was attached to the thoracic wall. Fasting activity was recorded for a 30 min period after an overnight fast.

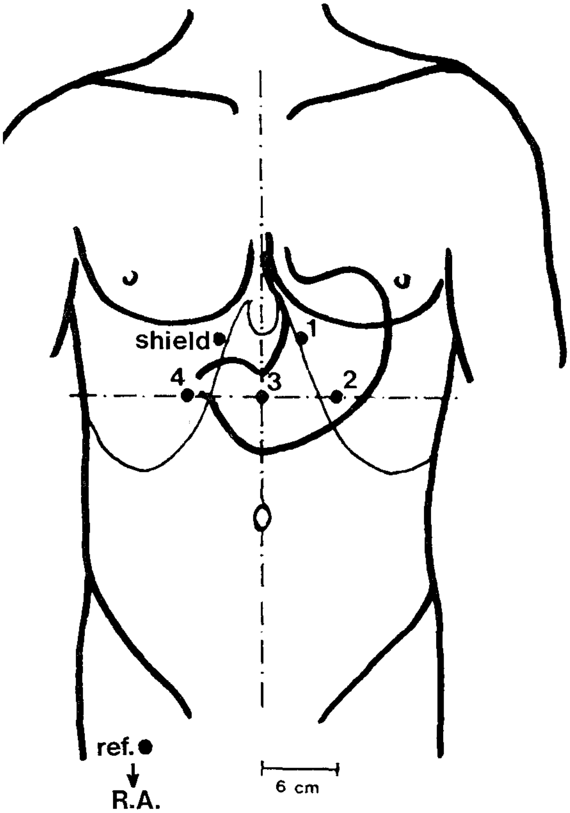


fig. 6.3.1 Electrode positions used in this study. Electrodes 2,3 and 4 are situated on a transverse line halfway between the lower end of the sternum and the umbilicus. Electrode 3 is placed at the intersection of this line and the median plane. The distance between all abdominal electrodes is 6 cm. Reference electrode is on the right ankle (RA). The shield electrode was used to reduce possible interference from the 50 Hz mains voltage at the input stage of the preamplifiers.

A test meal consisting of 250 ml of yoghurt with 20 g of sugar was then given, and consumed within 4 min, while the recording was continued. The composition of the test meal was: 8.75 g protein, 8.75 g fat and 30 g carbohydrate (990 kJ). The recording was stopped 35 min after the start of the test meal. Subjects lay quietly in a supine position during most of the recording session (only sitting up while eating the test meal). The 4 monopolar and 6 bipolar signals were recorded on paper (Van Gogh EP-8b) and simultaneously stored on magnetic tape (Racall Store 14). The high- and low-pass filters (6 decibel/octave) were set at 0.01 and 0.5 Hz respectively.

Signal analysis. A fast Fourier transform algorithm implemented on a NOVA 2 digital computer was used to obtain power spectra of the time signals. The signals, replayed from tape 16 times faster than real time, were preprocessed by band-pass filtering using a Butterworth filter (24 decibel/octave) with (real time) cut-off frequencies set at 0.01 and 0.5 Hz, to remove possible DC components and to avoid aliasing. They were then digitized (real time sampling frequency 1 Hz) and fed into the computer. The time signal of the whole recording period was used for signal analysis. Spectra were obtained as follows: every 64 s a power spectrum was computed from the preceding 256 s of the EGG time signal, to which a Hamming window had been applied to reduce leakage (26). These time values have been shown to enable the extraction of relevant information from the EGG, giving 129 points per spectrum and a frequency spacing of 0.0039 Hz (15). Tachygastrias which have a duration of at least 64 s can be detected using these time values (15). This procedure generates a series of overlapping spectra, called running spectra. They were plotted using grey-scale plots. Plots were made on a Versatec 1100 A printer plotter.

The mean gastric ECA frequency (in Hz), its standard deviation (GFSD) and its power content were computed for both the fasting and postprandial states.

The GFSD was used as a measure of the stability of the gastric ECA frequency. The larger the GFSD, the more unstable was the gastric ECA frequency in the period analysed.

Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance from the stomach wall) it is impossible to compare inter-individual or even intra-individual power data in separate recording sessions. Therefore in this study only power changes observed in one single recording session were used for analysis. To quantify the postprandial power change, the ratio of the power in the postprandial state to the power in the fasting state was computed. This is referred to as the Power Ratio (PR).

A tachygastria was considered to be present if a frequency about 2.5 to 3.5 times higher than the normal gastric ECA frequency could be recognized in the spectra, during a period in which the normal gastric ECA frequency was absent. Where it was considered to be necessary, running spectrum analysis of the respiration signal was performed to exclude confusion between frequencies of respiratory origin and possible tachygastrias.

Statistical analysis. Dichotomized data were compared using Fisher's exact test. The Wilcoxon signed-rank test was used to evaluate whether a significant difference existed between the myoelectrical behaviour before, 10 days after and 6 months after HSV. Probability (p) values were derived from two-tailed tests with 0.05 being taken as the significant level.

The study was approved by the Medical Ethics Committee of the Erasmus University, Rotterdam, on June 4th, 1982 and carried out with the informed consent of the subjects.

6.3.4 Results

Control subjects. The results from the 8 control subjects before and after cholecystectomy are summarized in table 6.3.1. The postoperative course was uncomplicated. None of the subjects had gastrointestinal complaints or medication on the days of the recording and all had consumed an unrestricted diet for 3 days.

Table 6.3.1. EGG parameters in the control group before operation, 10 days after and 6 months after operation.

	Control subjects n=8		
Fasting state	Before operation	10 days after operation	6 months after operation
Gastric ECA	0.051	0.050	0.051
frequency (Hz)	0.048–0.054	0.048–0.053	0.047–0.054
GFSD	0.0026	0.0025	0.0029
	0.0016–0.0032	0.0019–0.0039	0.0017–0.0040
Tachygastrias	0	0	0
Postprandial state			
Postprandial frequency dip	8	8	8
Gastric ECA	0.056	0.055	0.055
frequency (Hz)	0.050–0.059	0.051–0.059	0.050–0.060
GFSD	0.0020	0.0026	0.0021
	0.0016–0.0034	0.0019–0.0037	0.0017–0.0031
Power	6.57	5.38	7.16
ratio	2.65–10.54	2.78–9.89	3.32–12.06
Tachygastrias	0	0	0

Values represent median and range with the exception of tachygastrias and the postprandial frequency dip where the number of patients in whom this phenomenon is present is shown.

No changes were found in the myoelectrical behaviour after operation. In the fasting state a gastric ECA frequency of relatively low power was found, with negligible frequency variations in the grey-scale plot. Immediately after the test meal a dip in the gastric ECA frequency was observed in all patients. The average frequency decrease was 20% of the fasting ECA frequency. After about 5 min the ECA frequency started to increase again, generally resulting in a temporary overshoot. After that the ECA frequency, referred to as the postprandial ECA frequency, stabilized at a level which was somewhat higher than the fasting ECA frequency. Although there was a large variation between individuals, an increase in the power of the gastric ECA frequency after the test meal was seen in all patients. The frequency and power pattern shown in fig. 6.3.2 was representative for this group. No tachygastrias were detected before, 10 days after or 6 months after operation.

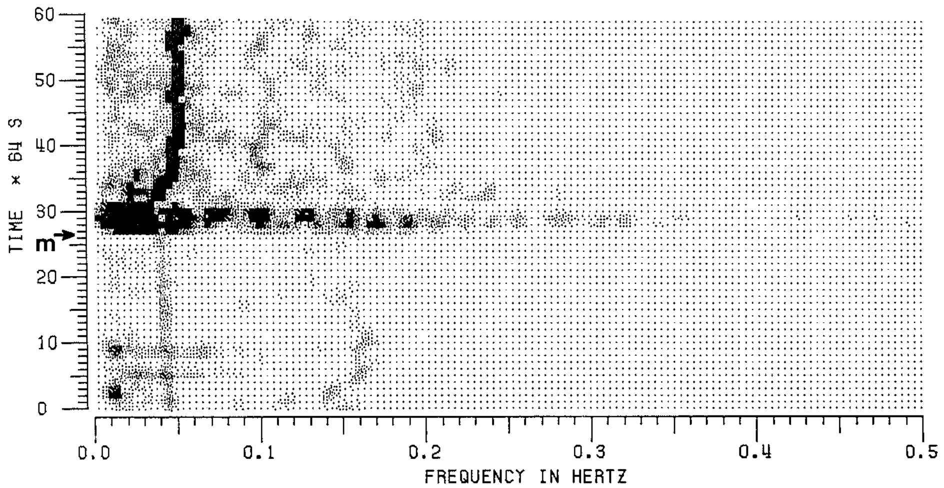


fig. 6.3.2 Grey-scale plot of an electrogastrogram showing frequency and power behaviour representative for the control group and for the HSV patients before and 6 months after operation. The degree of blackness is proportional to the magnitude of power of the EGG signal, divided into 36 distinct grey levels. Note the dip in the ECA frequency and the power increase following the test meal, marked with 'M'. The frequency band during the test meal is caused by motion artefacts, which in this patient was very pronounced.

The myoelectrical behaviour of the cholecystectomy patients was not essentially different, before or after operation, from the myoelectrical behaviour of HSV patients before operation as shown in the grey-scale plot of fig. 6.3.2.

Highly selective vagotomy patients. The results from the 12 patients before and after the HSV are summarized in table 6.3.2. The postoperative course was uncomplicated in 11 patients; none of them had gastrointestinal complaints and all had been on an unrestricted diet for at least 3 days. One patient complained of recurrent nausea and vomiting during the postoperative phase and was unable to consume the test meal on the tenth postoperative day. Five days later he was free of complaints. The response of the gastric acid output to hypoglycaemia had decreased by at least 75% decreased in all patients following the operation.

Table 6.3.2. EGG parameters in the patient group before operation, 10 days after and 6 months after operation.

	HSV patients		
Fasting state	Before operation n=12	10 days after operation n=11	6 months after operation n=12
Gastric ECA frequency (Hz)	0.050 0.047–0.052	0.050 0.048–0.051	0.053* 0.049–0.059
GFSD	0.0022 0.0017–0.0036	0.0024 0.0020–0.0034	0.0025 0.0018–0.0038
Tachygastrias	0	2	0
Postprandial state			
Postprandial frequency dip	12	0	12
Gastric ECA frequency (Hz)	0.053 0.049–0.056	0.050* 0.048–0.052	0.057* 0.051–0.063
GSFD	0.0026 0.0022–0.0038	0.0024 0.0020–0.0037	0.0028 0.0019–0.0041
Power ratio	5.64 2.86–10.56	1.21* 0.88–1.51	4.61 2.75–7.95
Tachygastrias	0	1	0

Values represent median and range with the exception of tachygastrias and the postprandial frequency dip where the number of patients in whom this phenomenon is present is shown.
p. value for the difference between groups:*: <0.01.

The myoelectrical behaviour before operation was identical to that of the control group. After HSV several abnormalities in the myoelectrical behaviour were observed.

Ten days after operation the fasting ECA frequency showed no changes. However, after 6 months a small but significant increase ($p<0.01$) in ECA frequency was found. The standard deviation (GFSD) of the ECA frequency did not change. In 3 patients tachygastrias were found 10 days after operation. In the patient who complained of nausea and vomiting and was unable to consume the test meal, a tachygastria was observed during the whole recording period (fig. 6.3.3). The durations of the tachygastrias in the other two patients were 3 and 5 minutes, respectively, in the fasting state and 4 minutes in the postprandial state (1 patient).

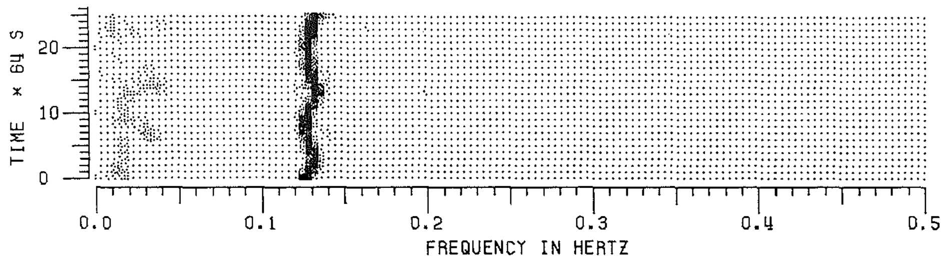


fig. 6.3.3 Grey-scale plot of the electrogastrogram of the HSV patient who complained of nausea and vomiting, with a tachygastria at about 0.12 Hz during the whole (fasting) recording period. Note that the normal gastric ECA frequency at about 0.05 Hz is absent.

On the tenth postoperative day no ECA frequency dip, or subsequent increase, was observed in the postprandial state. In fact the postprandial ECA frequency was somewhat lower than before operation ($p<0.01$). Six months after HSV the postprandial ECA frequency dip had returned, as had the slight postprandial ECA frequency increase over fasting values. A significant increase ($p<0.01$) in postprandial ECA frequency was found in comparison with the postprandial ECA frequencies before and 10 days after operation. The GFSD on the tenth postoperative day tended to be smaller, but this was not significant. However, the normal postprandial power increase of the gastric ECA frequency after the test meal (at least a factor 2 (22)) was not found on the tenth postoperative day. A power decrease, no change or only a small power increase was observed. This is expressed by the PR. The power behaviour was significantly different ($p<0.01$) with regard to values both before and 6 months after operation when the power behaviour had returned to normal.

The grey-scale plot of an electrogastrogram representative of the tenth postoperative day is shown in fig. 6.3.4. The myoelectrical behaviour and thus the grey-scale plots of the electrogastrograms of the HSV patients 6 months after operation were identical to those of the preoperative recordings.

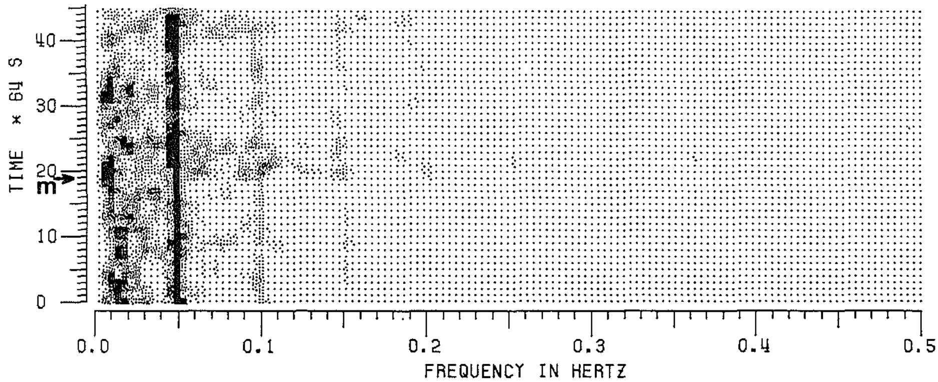


fig. 6.3.4 Grey-scale plot of a representative electrogastrogram of a HSV patient on the tenth postoperative day, showing the gastric ECA frequency at about 0.05 Hz. Note the absence of the frequency dip after the test meal (marked with 'M') and the small postprandial power change. The frequency at about 0.10 Hz is the second harmonic of the gastric ECA frequency and is a consequence of the signal analysis technique.

It should be noted that the patient who had nausea and vomiting on the tenth postoperative day recovered spontaneously. Four days later he was free of complaints and was on an unrestricted diet. The characteristics of the electrogastrogram on the 14th postoperative day were identical to those of the other patients on the 10th postoperative day.

6.3.5 Discussion

The preoperative values for the fasting and postprandial gastric ECA frequencies in both the control and the vagotomy groups are similar to previous measurements of gastric myoelectrical activity in a large population of healthy volunteers in our department (22), and correspond with values reported in the literature (7,11,15).

After highly selective vagotomy we observed several changes in gastric myoelectrical behaviour.

Ten days after highly selective vagotomy the most consistent finding was an absence of the normal changes in gastric ECA frequency following feeding: the normal initial dip, followed by an increase to a level higher than the fasting level, was not seen. In addition no or only a small postprandial power increase was observed, compared with the values for a normal population (22). Three patients had tachygastrias during the recording sessions.

Six months later the response to feeding was normal: the initial ECA frequency dip was followed by a slight increase in frequency with respect to the fasting level and there was a normal postprandial power increase. However, both the fasting and postprandial ECA frequencies were higher than before the operation or shortly after it.

It seems highly likely that these changes are due to the vagotomy and are not a result of the laparotomy, as they were not observed in patients undergoing a cholecystectomy.

Our findings, which showed a late increase in ECA frequency 6 months after vagotomy, are in agreement with those of Smallwood et al (27) and Barbara et al (1). Smallwood et al, who also used EGG, found an increase in gastric ECA frequency from 0.052 ± 0.004 Hz before operation to 0.057 ± 0.004 Hz after highly selective vagotomy (27).

Antral myoelectrical activity is basically myogenic in origin but is influenced by both neural and humoral stimuli. It has been previously suggested that the changes seen immediately after vagotomy in the fasting gastric myoelectrical activity, in particular the dysrhythmias, are due to temporary imbalance between the vagal and sympathetic innervation of the stomach (2,9). Ten days after HSV one could expect more dysrhythmias than 6 months after HSV, by which time a gradual adaptation to this altered autonomic innervation has taken place. This is in agreement with our results. Tachygastrias were only observed 10 days after HSV.

Tachygastrias following vagotomy have also been observed by others (2,3,5,9). It is noteworthy that the incidence in our study is less than reported by Stoddard et al (9), who found tachyarrhythmias and tachygastrias in all patients after HSV. With regard to the present study it should be realized that EGG has its limitations in detecting tachygastrias shorter than 64 seconds (15). However, in patients with unexplained nausea and vomiting a similar difference between the incidence of tachygastrias when recorded with peroral suction electrodes (28) and the incidence when measured with EGG (22) has been observed, which suggests that mucosal suction electrodes may give rise to tachygastrias, in particular in the diseased state.

Stoddard et al found no causal relationship between tachygastrias and complaints (9). The number of patients with tachygastrias in our series is too small to allow firm conclusions. However, the improvement in symptoms and normalisation of the myoelectrical behaviour in the single patient in whom the tachygastria (and associated with nausea and vomiting) was present during the whole recording period on the tenth postoperative day, suggests a causal relationship. Tachygastrias of short duration are probably not associated with complaints.

The motor correlate of the abnormal myoelectrical behaviour observed with EGG is still not fully understood. From previous studies (13,16,21) it is known that a power increase of the gastric ECA frequency indicates the presence of ERA and thus motor activity. The absence of the normal postprandial power increase 10 days after HSV suggests that the customary gastric feeding pattern has not been resumed while the normalisation of the power behaviour after 6 months suggests that this change is reversible. It has been proposed that vagal integrity is necessary for the normal gastric feeding pattern to occur. Both truncal and highly selective vagotomy have been found to disrupt gastric motility and to delay gastric emptying (6,29,30). Furthermore there is evidence that the disturbance of postprandial gastric motility produced by vagotomy often recovers with time (31). Hall et al (32) recently confirmed this hypothesis by demonstrating in dogs that the vagus nerves are essential for the initiation and maintenance of postprandial motor activity in the stomach. During (truncal) vagotomy induced by cooling, feeding does not interrupt the interdigestive motor pattern. Normal cycles of the interdigestive migrating complex (IMC) were seen in the postprandial state after vagotomy. If the same phenomenon occurs in man after HSV this would explain the power behaviour 10 days after operation. The fact that the power ratio ranges from 0.88 to 1.51 can then be understood, if one realizes that each phase of the IMC has a different power level and that the duration of an IMC cycle is relatively long with respect to the recording period (30 min) in this study (21). The apparent reappearance of the feeding pattern several months after vagotomy, suggested by our results and by those of other authors (29,30), could possibly be due to adaptive mechanisms not normally responsible for gastric motility which act as substitutes for the vagus nerves (32). Another explanation could be that the function of the remaining vagal nerves is impaired by the operation and that on the tenth postoperative day they have not yet recovered from manipulation during operation.

The control mechanisms and motor correlate of the postprandial ECA frequency dip are still unknown but this study suggests a role for the vagus nerves.

In conclusion, it can be said that highly selective vagotomy is associated with changes in the myoelectrical behaviour, in particular in the postprandial state, which are partly reversible with time. The changes in the power response could well be associated with a temporary failure in HSV patients to convert the interdigestive motility pattern into a feeding pattern. Much of the myoelectrical behaviour of the stomach is still not understood. Further investigation of myoelectrical and motor activity, in particular in the postprandial state, in patients with various disorders (including patients undergoing highly selective vagotomy) should help unravel the (patho)physiology of gastric motility.

6.3.6 References

1. Barbara L., Bortolotti M., Vezzadani P., Serantoni C., Ciani P.A., Miglioli M., Labo G. Electrical and mechanical activity of the stomach, serum gastrin levels and acid secretion before and after selective proximal vagotomy for duodenal ulcer. Rendic. Gastroent. 1973; 5: 17-18.
2. Stoddard C.J., Smallwood R., Brown B.H., Duthie H.L. The immediate effects of different types of vagotomy on human gastric myoelectrical activity. Gut 1975; 16:165-170.
3. Bortolotti M., Labo G., Serantoni C., Ciani P. Effects of highly selective vagotomy on gastric motor activity of duodenal ulcer patients. Digestion 1978; 17: 108-120.
4. Lavigne M.E., Wiley Z.D., Martin P., Way L.W., Meyer J.H., Sleisenger M.H., MacGregor I.L. Gastric, pancreatic, and biliary secretion and the rate of gastric emptying after parietal cell vagotomy. Am. J. Surg. 1979; 138: 644-651.
5. Aldrete J.S., Shepard R.B., Halpern N.B., Jimenez H., Piantadosi S. Effects of various operations on the electrical activity of the human stomach recorded during the postoperative recovery period. Ann. Surg. 1982: 662-668.
6. Wittebol P., Akkermans L.M.A., Hulstaert P.F. Prognostic factors in surgery for duodenal ulcer. In: Nyhus L.M., ed. Surgery Annual 1985. Crofts, USA: Appleton Century, 1985: 235-247.
7. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transsection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.
8. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
9. Stoddard C.J., Smallwood R.H., Duthie H.L. Electrical arrhythmias in the human stomach. Gut 1981; 22: 705-712.
10. Thouvenot J., Tonkovic S., Penaud J. Electrosplanchnography: Method for electrophysiological exploration of the digestive tract. Acta Med. Iugosl. 1973; 27: 227-247.
11. Brown B.H., Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from

surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.

12. Smallwood R.H., Brown B.H., Duthie H.L. An approach to the objective analysis of intestinal smooth muscle potentials recorded from surface electrodes. In: Vantrappen G., ed. Proc. 5th Int. Symposium on Gastrointestinal Motility, Leuven. Belgium. Typoff-Press, 1975: 248-253.
13. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. What is measured in electrogastrography? Dig. Dis. Sci. 1980; 25: 179-187.
14. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. Postprandial and interdigestive gastric electrical activity in the dog recorded by means of cutaneous electrodes. In: Christensen J., ed. Gastrointestinal motility. New York: Raven Press, 1980: 187-194.
15. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals recorded from dogs and man. In: Wienbeck M., ed. Motility of the digestive tract. New York: Raven Press, 1982: 241-250.
16. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.
17. Abell T., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in humans shown by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.
18. Hamilton J.W., Bellahsene B.E., Reichelderfer M., Webster J.G., Bass P. Human electrogastrograms, comparison of surface and mucosal recordings. Dig. Dis. Sci. 1986; 31: 33-39.
19. Geldof H., Van der Schee E.J., Grashuis J.L. Accuracy and reliability of electrogastrography. (abstr.) Gastroenterology 1986; 90: 1425.
20. Geldof H., Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Electrogastrography. In: Akkermans L.M.A., Johnson A.G., Read N.W. eds. Gastric and gastroduodenal motility. New York: Praeger Publishers, 1984: 163-175.
21. Geldof H., Van der Schee E.J., Grashuis J.L. Electrogastrographic characteristics of interdigestive

migrating complex in humans. Am. J. Physiol. 1986; 250 (Gastrointest. Liver Physiol. 13): G165-G171.

22. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting. Gut 1986; 27: 799-808.
23. Goligher J.C. A technique for highly selective (parietal cell or proximal gastric) vagotomy for duodenal ulcer. Brit. J. Surg. 1974; 61: 337-345.
24. Mirizzi N., Scafoglieri U. Optimal directions of the electrogastrographic signal in man. Med. Biol. Eng. Comp. 1983; 21: 385-389.
25. Smout A.J.P.M., Van der Schee E.J., Akkermans L.M.A., Grashuis J.L. Recording of gastrointestinal activity from surface electrodes. Scand. J. of Gastroenterol. 1984; 19: suppl. 96: 11-18.
26. Blackman R.B., Tuckey J.W. The measurement of power spectra. Dover Publications Inc. New York, 1958.
27. Smallwood R.H. Gastrointestinal electrical activity from surface electrodes. Thesis, 1976, Sheffield, England.
28. Chey W.J., You C.H., Lee K.Y. Menguy R. Gastric Dysrhythmia: clinical aspects. In: Chey W.J. ed. Functional disorders of the digestive tract. New York: Raven Press, 1983: 175-181.
29. Malagelada J-R., Rees W.D.W., Mazzotta L.J., Go V.L.W. Gastric motor abnormalities in diabetic and postvagotomy gastroparesis; effect of metoclopramide and bethanechol. Gastroenterology 1980; 78: 286-293.
30. McCrea E.D., McSwiney B.A., Stopford J.S.B. The effect on the stomach of section of the vagi nerves. Q. J. Exp. Physiol. 1926; 16: 195-203.
31. Ruckebusch Y., Bueno L. Migrating myoelectrical comlex of the small intestine: an intrinsic activity mediated by the vagus. Gastroenterology 1977; 73: 1309-1314.
32. Hall K.E., El-Sharkawy T.Y., Diamant N.E. Vagal control of canine postprandial upper gastrointestinal motility. Am. J. Physiol. 1986; 250 (Gastrointest. Liver Physiol. 13): G501-G510.

6.4 GASTRIC MYOELECTRICAL ACTIVITY AND SOLID FOOD EMPTYING FOLLOWING HIGHLY SELECTIVE VAGOTOMY IN PATIENTS WITH AND WITHOUT NAUSEA AND VOMITING

Submitted for publication.
Co-authors E.J. van der Schee, M. van Blankenstein, L.M.A. Akkermans, A.J.P.M. Smout.

6.4.1 Abstract

Gastric myoelectrical activity and gastric emptying of a solid meal were studied following highly selective vagotomy in 28 patients both with (16) and without (12) postprandial nausea and vomiting. Gastric myoelectrical activity was recorded by electrogastrography. Gastric emptying was studied by using a radiolabelled solid phase meal. In general no abnormal myoelectrical behaviour was seen in patients without symptoms. Abnormal myoelectrical activity was observed in 81% of the patients with symptoms of nausea and vomiting after highly selective vagotomy. This was characterized in the electrogastrogram by: 1) the absence of the normal initial decrease in the frequency of the postprandial electrical control activity (which was not correlated with abnormal gastric emptying); 2) the absence of the normal postprandial increase in the amplitude of the gastric electrical control activity (which was correlated with a delayed gastric emptying for a solid meal). Both changes indicate postprandial antral hypomotility. Tachygastrias were observed only in 2 symptomatic patients and in 1 asymptomatic patient, who had normal gastric emptying.

6.4.2 Introduction

Highly selective vagotomy (HSV), also known as proximal gastric vagotomy, was introduced on the assumption that by preserving the innervation of the antroduodenal junction many of the motility disturbances caused by truncal and selective vagotomy could be prevented. In this respect the operation appears to be successful as the incidence of dumping and diarrhoea is greatly reduced (1). Whether other symptoms, such as the feeling of fullness, nausea and vomiting, which sometimes follow truncal or selective vagotomy, have also been reduced is not so certain. Gastric motility disturbances have been described after HSV (2-8).

One of the most important control mechanisms of gastric motility is electrical in nature. The smooth muscle cells of the aboral two-thirds of the stomach generate cyclically recurring electrical potentials. These constantly present, periodic potentials have been called slow waves, basic electrical rhythm, or, as in this study, electrical control activity (ECA) (9,10). When motor activity is present the ECA is accompanied by a second component, with or without superimposed fast oscillating potential changes (spikes or spike activity), referred to as electrical response activity (ERA) (10).

Studies of gastric myoelectrical behaviour after HSV have given conflicting results concerning the relationship between abnormal myoelectrical activity and symptoms (2-4,11). Most of the studies were undertaken using peroral mucosal suction electrodes or serosal electrodes placed at laparotomy and recordings were made only in the fasting state. However, the postprandial state seems to be more important when studying the relation between symptoms and myoelectrical activity.

Gastric myoelectrical activity can be recorded in a non-invasive way by means of electrodes attached to the abdominal skin, a method called electrogastrography (EGG). EGG allows the recording of gastric myoelectrical activity in both the fasting and postprandial states, providing information about the gastric ECA frequency, ECA arrhythmias and the presence of ERA (12-21).

In the present study gastric myoelectrical activity was recorded by means of EGG, in both the fasting and postprandial states in HSV patients with and without nausea and vomiting. Gastric emptying of solids was also measured to determine whether changes in myoelectrical behaviour were associated with delayed gastric emptying.

6.4.3 Methods

Subjects. Twenty-eight patients participated in the study. In all patients HSV had been carried out for duodenal ulceration 1 to 6 years before to the study. HSV was performed according to accepted techniques (22). Reduction (by more than 85%) in gastric acid output after stimulation by insulin-induced (0.15 IU/kg) hypoglycaemia was used to demonstrate the completeness of the vagotomy. Twelve patients (8 men and 4 women, mean age 41, range 31 - 59) were free of symptoms suggestive of gastric motor disturbances. Sixteen patients (12 men and 4 women, mean age 39, range 27 - 60) complained of frequent (more than three times a week) postprandial nausea and vomiting, accompanied by one or more of the following symptoms: belching, abdominal distension, sense of fullness after a normal meal and/or inability to finish a normal meal. The diagnostic workup included an upper gastrointestinal endoscopy to ensure that there was no recurrent ulcer disease and/or pyloric stenosis.

Technique of the gastric emptying study. In all patients gastric emptying was studied using a radioactive labelled solid-phase meal (a pancake) as described by Akkermans et al (23) and Jacobs et al (24,25). Both the lag-phase and the percentage emptied in one hour were used to describe the gastric emptying. In normal healthy volunteers (n=12) a lag-phase of 22.2 ± 6 minutes (mean ± SD) and an emptying rate of 57 ± 12.5 (mean ± SD) was found (25). Patients were considered to be abnormal if these measurements exceeded the mean of the control subjects by more than two standard deviations.

Technique of EGG recording. Gastric myoelectrical activity was recorded by means of cutaneous electrodes as described by Van der Schee et al (16), Smout et al (26) and Geldof et al (18,27,28). Fasting activity was recorded for a 30 min period after an overnight fast. A test meal consisting of 250 ml of yoghurt with

20 g of sugar was then given, and consumed within 4 min, while the recording was continued. The composition of the test meal was: 990 kJ, 8.75 g protein, 8.75 g fat and 30 g carbohydrate. The recording was stopped 35 min after the start of the test meal. Subjects lay quietly in a supine position during most of the recording session (only sitting up while taking the test meal).

Signal analysis. Signal analysis was performed using running spectrum analysis, based on a fast Fourier transform, as described by Van der Schee et al (16) and Geldof et al (18,27,28). Tachygastrias which have a duration of at least 64 s can be detected using this method (16). The procedure generates a series of overlapping spectra, called running spectra, which are plotted using grey-scale plots. In a grey-scale plot the degree of blackness is proportional to the magnitude of the power of the electrogastrographic signal. The blackness is divided into 36 distinct grey levels.

The mean gastric ECA frequency (Hz) with its standard deviation (GFSD) and its power content were computed for both the fasting and postprandial states. The GFSD was used as a measure of the stability of the gastric ECA frequency. The larger the GFSD, the more unstable was the gastric ECA frequency in the period analysed.

Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content, the amplitude being the square root of the power) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance from the stomach wall), it is impossible to make a comparison of inter-individual and even intra-individual power data. Therefore in this study only power changes of the gastric ECA frequency in one single recording session were used for analysis. To quantify the postprandial power change, the ratio of the power in the postprandial state to the power in the fasting state was computed and referred to as the power ratio (PR).

A tachygastria was considered to be present if a frequency about 2.5 to 3.5 times higher than the normal gastric ECA frequency could be recognized in the spectra, during a time period in which the normal gastric ECA frequency was absent. Where it was considered to be necessary, running spectrum analysis of the respiration signal was performed to exclude confusion between frequencies of respiratory origin and possible tachygastrias.

Statistical analysis. Dichotomized data were compared using Fisher's exact test. To compare continuous data between the groups the Mann-Whitney U-test (non-parametric) was used. Probability (p) values were derived from two-tailed tests with 0.05 being taken as the significant level.

The study was approved by the Medical Ethics Committee of the Erasmus University, Rotterdam, on June 4, 1982 and carried out with the informed consent of the subjects.

Table 6.4.1. EGG parameters in asymptomatic and symptomatic HSV patients.

	Without symptoms n=12	With symptoms n=16
Fasting state		
Gastric ECA frequency (Hz)	0.050 0.045–0.059	0.052 0.041–0.059
GFSD	0.0027 0.0019–0.0047	0.0025 0.0020–0.0036
Tachygastrias	1	0
Postprandial state		
Postprandial frequency dip	12	9
Gastric ECA frequency (Hz)	0.058 0.051–0.062	0.055 0.036–0.060
GFSD	0.0033 0.0025–0.0051	0.0029 0.0022–0.0050
Power ratio	4.46 1.73–8.58	2.15* 0.50–9.60
Tachygastrias	1	0
Gastric emptying		
Normal	11	9
Delayed	1	7

Values represent median and range with the exception of the tachygastrias, the postprandial frequency dip and gastric emptying results (number of patients). p-value for the difference between groups:*: <0.02.

6:4.4 Results

In the group of patients studied, 12 were free of symptoms. Only 1 of these asymptomatic patients had delayed gastric emptying. Sixteen patients complained of nausea and vomiting and various associated symptoms. Of these 16 patients with symptoms, 7 had delayed gastric emptying (table 6.4.1).

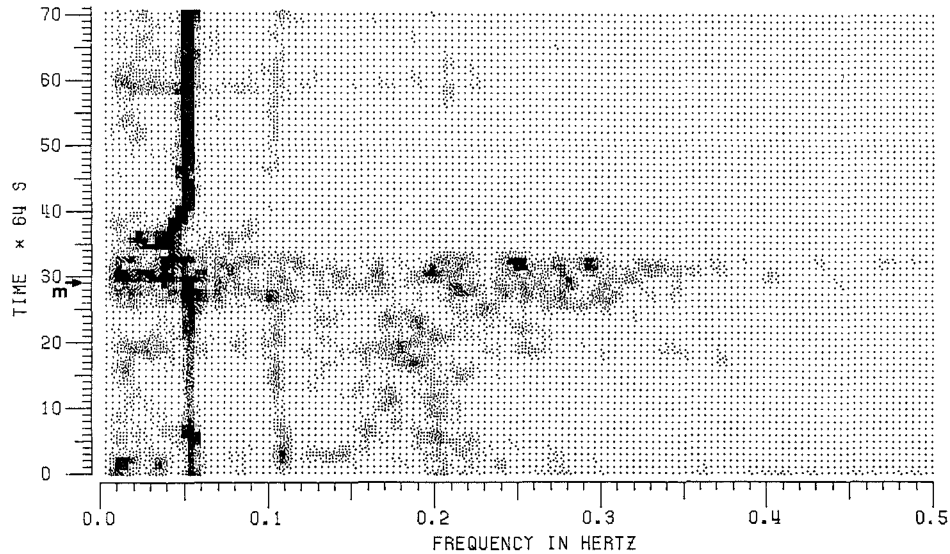


fig. 6.4.1 Grey-scale plot of a typical electrogastrogram for an HSV patient without symptoms. Note the postprandial frequency dip and the power increase, expressed by the increase in blackness of the gastric ECA frequency component. Test meal marked with "M". The frequency band during the meal is caused by motion motion artefacts. Frequency at about 0.11 Hz is the second harmonic of the gastric ECA frequency, a consequence of the signal analysis technique.

The delayed gastric emptying in 6 patients was due to a slow emptying rate ranging from 18 to 30% with a normal lag-phase of 12 to 42 min. In 1 of these patients it was due to both a slow emptying rate (26%) and a longer lag-phase (92 min). In the seventh patient the emptying rate was 36%, close to the lower limit of normal, and the 70 min lag-phase was longer than normal.

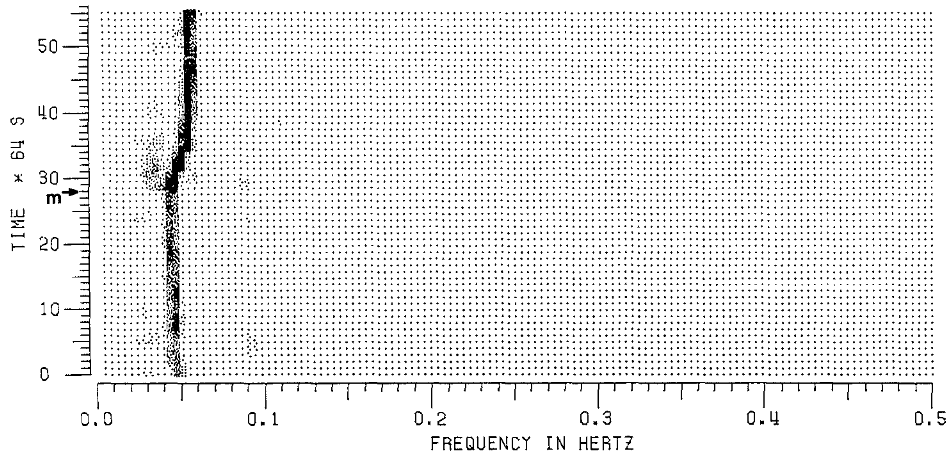


fig. 6.4.2 Grey-scale plot of the electrogastrogram of an HSV patient in whom the normal gastric ECA frequency dip immediately after the test meal is absent. Test meal marked with "M".

The myoelectrical behaviour in the asymptomatic patients is summarized in table 6.4.1. In the fasting state a gastric ECA frequency of relatively low power with, in the majority of the patients, negligible frequency variations, was seen in the grey-scale plots. Immediately after the test meal a dip in the gastric ECA frequency was observed in these 12 patients. The average frequency decrease was 18% of the fasting ECA frequency. After about 5 to 6 min the ECA frequency started to increase again, generally resulting in a temporary overshoot. After that the ECA frequency, referred to as the postprandial frequency, stabilized at a level which was equal to or somewhat higher than the fasting ECA frequency. In 11 of these patients the power of the gastric ECA frequency after the test meal was at least 2.23 times higher than before the meal. In the remaining patient a PR of 1.73 was found. The frequency and power pattern shown in fig. 6.4.1 was representative for this group. Two short tachygastrias (3 and 5 min respectively) were observed in patients in this group.

Table 6.4.2. EGG parameters in asymptomatic and symptomatic HSV patients with normal and delayed gastric emptying.

	Gastric emptying	
	Normal n=20	Delayed n=8
Fasting state		
Gastric ECA frequency (Hz)	0.051 0.045–0.059	0.050 0.041–0.056
GFSD	0.0027 0.0019–0.0038	0.0029 0.0024–0.0047
Tachygastrias	1	0
Postprandial state		
Postprandial frequency dip	16	5
Gastric ECA frequency (Hz)	0.057 0.049–0.062	0.053 0.036–0.058
GFSD	0.0027 0.0022–0.0035	0.0041 0.0032–0.0051
Power ratio	4.12 0.96–9.60	0.96* 0.50–1.73
Tachygastrias	1	0

Values represent median and range with the exception of the tachygastrias, the postprandial frequency dip (the number of patients).
p-value for the difference between groups: *: < 0.005.

The myoelectrical behaviour in 13 of the 16 symptomatic patients differed from the asymptomatic group (table 6.4.1). In 7 patients there was no initial decrease in the postprandial ECA frequency, as can be seen in fig. 6.4.2. There were no significant differences between these patients and those without symptoms as far as the overall gastric ECA frequency values and the stability of the gastric ECA frequency were concerned. In 9 symptomatic patients the postprandial power behaviour was, however, different. No power increase, a small power increase, or even a small power decrease was observed in these patients after the test meal (fig. 6.4.3). The small PR for these 9 patients, ranging between 0.50 and 1.46, is responsible for the significant difference between the PR in symptomatic and asymptomatic patients. It was remarkable that no tachygastrias were observed in the symptomatic group.

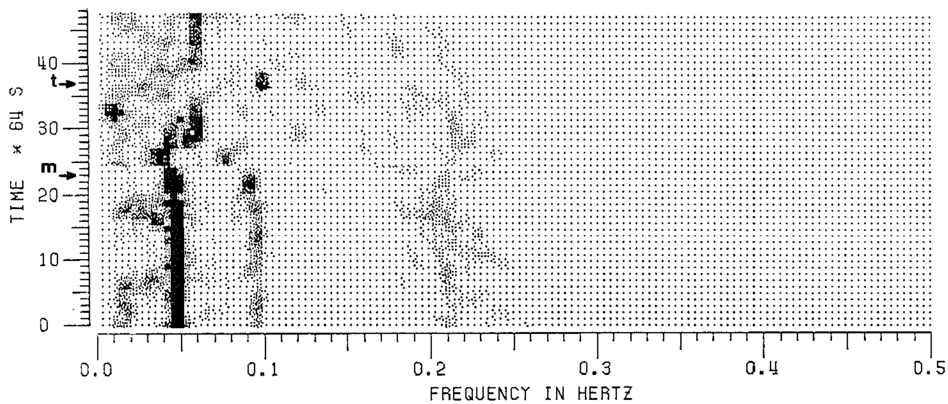


fig. 6.4.3 Grey-scale plot of the electrogastrogram of an HSV patient with nausea and vomiting and delayed gastric emptying of solids. In the fasting state a second harmonic is present. Test meal marked with "M". Note the absence of the postprandial power increase. In the postprandial state a tachygastria is seen marked with 't' (note that the normal gastric ECA frequency at about 0.05 Hz is absent). Frequencies at about 0.21 Hz are of respiratory origin.

A comparison was made of the myoelectrical behaviour of patients with normal and with delayed gastric emptying to study if there was any relationship between abnormal myoelectrical activity and the gastric emptying pattern (table 6.4.2). No distinction could be made between delayed gastric emptying due to a slow emptying rate and that due to an exceptionally long lag-phase, because there were not many occurrences of the latter. Only the PR showed a significant difference. In all 8 patients with delayed gastric emptying (7 symptomatic and 1 asymptomatic, the PR in this patient being 1.73) no increase, a small increase, or even a decrease in the postprandial power was observed. In the group with normal gastric emptying a small PR (0.96 and 1.16) was observed in 2 symptomatic patients in whom the gastric emptying rate was close to the lower limit of normal. The PR in the remaining 18 patients with normal gastric emptying was at least 2.23. The absence of the postprandial frequency dip was equally divided over both groups. It should be noted that normal gastric emptying was found in the patients with a tachygastria.

6.4.5 Discussion

The values for the fasting and postprandial gastric electrical control activity (ECA) frequencies in HSV patients correspond to values for healthy control subjects reported in the literature (9,12,16,27). In the majority of patients a stable gastric ECA frequency, expressed by a GFSD of less than 0.0035, was observed. Patients with an unstable gastric ECA frequency (GFSD larger than 0.0035 indicative of frequency variations of at least 0.008 Hz) were equally divided over the groups. As the control mechanisms and the motor correlate of the reduction in gastric ECA frequency immediately after a test meal is not completely understood and as there was no correlation with either normal or delayed gastric emptying, no conclusions can be drawn from the absence of the postprandial dip in some patients. One could suggest that in these patients denervation of the gastric pacemaker is responsible. The fact that the postprandial frequency dip was only absent in patients with symptoms suggestive of a motility disorder and the fact that in a healthy control population this frequency dip was present in every subject (27), emphasizes the importance of further study into this phenomenon. The incidence of tachygastrias was in our study lower than that reported by Stoddard et al (11). However, EGG with running spectrum analysis used in the present study has its limitations in the detection of tachygastrias shorter than 64 seconds (16). The finding that the 2 patients in whom a tachygastria was observed had no symptoms is consistent with the findings of Stoddard et al. (11) who also failed to find a relation between tachygastrias and nausea and vomiting.

The characteristic abnormality found in the electrogastrograms of symptomatic HSV patients was the absence of the normal postprandial power increase. In a group of 52 healthy volunteers a power increase of at least a factor 2 (PR>2.00) was observed (27). The normal postprandial power increase in the gastric ECA frequency is ascribed to the additional contribution of ERA to the signal during motor activity (14,17,28). The lack of or diminished postprandial motor activity, and thus the absence or reduction of ERA, could be responsible for the absence of the normal postprandial power increase. Grinding and emptying of solids are primarily a function of the gastric antrum (29-32) and the rate of gastric emptying of solids is proportional to phasic antral pressure activity induced by the meal (33). As it is antral myoelectrical activity in particular that is recorded by EGG (17,18,26), the finding that the absence of the normal postprandial power increase coincides with delayed gastric emptying of solids in HSV patients indeed seems to suggest a decrease in postprandial ERA. A similar correlation between delayed gastric emptying of solids and the absence of the normal postprandial power increase has also been observed in patients with chronic unexplained nausea and vomiting (27). An explanation for the suspected antral hypomotility could be that the vagotomy was too extensive.

In conclusion, abnormal myoelectrical activity was rare in HSV patients who had no symptoms. In 81% of the symptomatic patients abnormal myoelectrical activity was observed in the electrogastrogram, characterized by: 1) the absence of the normal initial postprandial ECA frequency decrease; 2) the absence of the normal postprandial power increase in the gastric ECA. This latter abnormality is correlated with delayed gastric emptying of a solid meal, which is indicative of postprandial antral hypomotility. Only a few tachygastrias were observed in this study and they do not seem to play a major role in the production of symptoms. The finding that gastric emptying of solids and gastric myoelectrical activity were normal in a substantial proportion of HSV patients with postprandial symptoms of nausea and vomiting indicates that other mechanisms are involved and emphasizes the need for further investigation into the pathogenesis of these symptoms.

6.4.6 References

1. Sheiner H.J. Gastric Motility. In: Duthie H.L., Wormsley K.G., eds. Scientific Basis of Gastroenterology. Churchill, Livingstone, 1976: 440-459.
2. Barbara L., Bortolotti M., Vezzadani P., Serantoni C., Ciani P.A., Miglioli M., Labo G. Electrical and mechanical activity of the stomach, serum gastrin levels and acid secretion before and after selective proximal vagotomy for duodenal ulcer. Rendic. Gastroent. 1973; 5: 17-18.
3. Stoddard C.J., Smallwood R., Brown B.H., Duthie H.L. The immediate effects of different types of vagotomy on human gastric myoelectrical activity. Gut 1975; 16:165-170.
4. Bortolotti M., Labo G., Serantoni C., Ciani P. Effects of highly selective vagotomy on gastric motor activity of duodenal ulcer patients. Digestion 1978; 17: 108-120.
5. Lavigne M.E., Wiley Z.D., Martin P., Way L.W., Meyer J.H., Sleisenger M.H., MacGregor I.L. Gastric, pancreatic, and biliary secretion and the rate of gastric emptying after parietal cell vagotomy. Am. J. Surg. 1979; 138: 644-651.
6. Storey D.W., Boulos P.B., Ward M.W.M., Clark C.G. Proximal gastric vagotomy after five years. Gut 1981; 22: 702-708.
7. Aldrete J.S., Shepard R.B., Halpern N.B., Jimenez H., Piantadosi S. Effects of various operations on the electrical activity of the human stomach recorded during the postoperative recovery period. Ann. Surg. 1982; ?: 662-668.
8. Wittebol P., Akkermans L.M.A., Hulstaert P.F. Prognostic factors in surgery for duodenal ulcer. In: Nyhus L.M., ed. Surgery Annual 1985. Crofts, USA: Appleton Century, 1985: 235-247.
9. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transsection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.
10. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
11. Stoddard C.J., Smallwood R.H., Duthie H.L. Electrical arrhythmias in the human stomach. Gut 1981; 22: 705-712.

12. Brown B.H., Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.
13. Smallwood R.H., Brown B.H., Duthie H.L. An approach to the objective analysis of intestinal smooth muscle potentials recorded from surface electrodes. In: Vantrappen G., ed. Proc. 5th Int. Symposium on Gastrointestinal Motility, Leuven. Belgium. Typoff-Press, 1975: 248-253.
14. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. What is measured in electrogastrography? Dig. Dis. Sci. 1980; 25: 179-187.
15. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. Postprandial and interdigestive gastric electrical activity in the dog recorded by means of cutaneous electrodes. In: Christensen J., ed. Gastrointestinal motility. New York: Raven Press, 1980: 187-194.
16. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals recorded from dogs and man. In: Wienbeck M., ed. Motility of the digestive tract. New York: Raven Press, 1982: 241-250.
17. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.
18. Geldof H., Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Electrogastrography. In: Akkermans L.M.A., Johnson A.G., Read N.W. eds. Gastric and gastroduodenal motility. New York: Praeger Publishers, 1984: 163-175.
19. Abell T., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in humans shown by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.
20. Hamilton J.W., Bellahsene B.E., Reichelderfer M., Webster J.G., Bass P. Human electrogastrograms, comparison of surface and mucosal recordings. Dig. Dis. Sci. 1986; 31: 33-39.
21. Geldof H., Van der Schee E.J., Grashuis J.L. Accuracy and reliability of electrogastrography. (abstr.) Gastroenterology 1986; 90: 1425.

22. Goligher J.C. A technique for highly selective (parietal cell or proximal gastric) vagotomy for duodenal ulcer. Brit. J. Surg. 1974; 61: 337-345.
23. Akkermans L.M.A., Jacobs F., Oei Hong You, Roelofs J.M.M., Wittebol P. A non-invasive method to quantify antral contractile activity in man and dog (a preliminary report). In Christensen J., ed. Gastrointestinal motility. New York: Raven Press, 1980: 195-202.
24. Jacobs F., Akkermans L.M.A., Oei Hong You, Hoekstra A., Wittebol P. Effects of domperidone on gastric emptying of semi-solid and solid food. In Towse G., ed. Progress with domperidone, a gastrokinetic and anti-emetic agent. London: Academic press, 1981: 11-20.
25. Jacobs F., Akkermans L.M.A., Oei Hong You, Hoekstra A., Wittebol P. A radioisotope method to quantify the function of fundus, antrum, and their contractile activity in gastric emptying of a semi-solid and solid meal. In: Wienbeck M., ed. Motility of the digestive tract. New York: Raven Press, 1982: 233-240.
26. Smout A.J.P.M., Van der Schee E.J., Akkermans L.M.A., Grashuis J.L. Recording of gastrointestinal activity from surface electrodes. Scand. J. of Gastroenterol. 1984; 19: suppl. 96: 11-18.
27. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting. Gut 1986; 27: 799-808.
28. Geldof H., Van der Schee E.J., Grashuis J.L. Electrogastrographic characteristics of interdigestive migrating complex in humans. Am. J. Physiol. 1986; 250: G165-G171.
29. Dozois R.R., Kelly K.A., Code C.F. Effect of distal antrectomy on gastric emptying of liquids and solids. Gastroenterology 1971; 61: 675-681.
30. Mroz C.T., Kelly K.A. The role of the extrinsic antral nerves in the regulation of gastric emptying. Surg. Gynecol. Obstet. 1977; 145: 369-377.

31. Hinder R.A., Kelly K.A. Canine gastric emptying of solids and liquids. Am. J. Physiol. 1977; 233: E335-E340.
32. Rees W.D.W, Miller L.J., Malagelada J-R. Dyspepsia, antral motor dysfunction, and gastric stasis of solids. Gastroenterology 1980; 78: 360-365.
33. Camilleri M, Brown M.L., Becker G., Zinsmeister A.R., Malagelada J-R. Relationship between antral pressure activity and gastric emptying in man. (abstr.) Dig. Dis. Sci. 1984; 29: 564.

6.5 AN ELECTROGASTROGRAPHIC STUDY OF GASTRIC MYOELECTRICAL ACTIVITY IN DUODENAL ULCER PATIENTS

6.5.1 Introduction

Little is known about gastric motility in duodenal ulcer patients. Alteration in gastric emptying has been implicated in duodenal ulcer disease, but the precise abnormalities remain controversial. Gastric emptying time for liquid and solid meals has been reported as normal or shortened in patients with an active duodenal ulcer (35,44). Myoelectrical activity plays an important role in the control of gastrointestinal motility, therefore investigation of gastric myoelectrical activity in duodenal ulcer patients may be helpful in identifying gastric motor disturbances.

In the present study gastric myoelectrical activity was recorded by EGG in patients with an active duodenal ulcer.

6.5.2 Materials and methods

Fourteen patients (10 men, 4 woman) median age 34 yrs (range 22-49) with a duodenal ulcer were studied. The 14 duodenal ulcer patients all had an endoscopically confirmed duodenal ulcer of at least 5 mm before the recording, and none had clinical or endoscopic evidence of pyloric stenosis. No patient recieved medication for 48 hours before the recording.

The study was approved by the Medical Ethics committee of the Erasmus University, Rotterdam, on June 4, 1982 and carried out with the informed consent of the subjects.

The recording techniques are described in the sections 4.2 and 4.4. The methods used for signal analysis and data presentation are identical to that described in section 4.3.

Statistical analysis. The Wilcoxon signed-rank-test was used to evaluate whether a significant difference existed between the EGG parameters of duodenal ulcer patients and the control group (described in section 5.3). The level of significance used in this study was 0.05.

6.5.3 Results

The results in the duodenal ulcer patients are summarized in table 6.5.1. and 6.5.2. No significant differences in myoelectrical behaviour were found between the patients with an active duodenal ulcer and the control group described in section 5.3.

Table 6.5.1. EGG parameters in duodenal ulcer patients.

	n=14	
	median	range
Fasting state		
Frequency (Hz)	0.046	0.042–0.050
Standard deviations (SD)	0.0025	0.0017–0.0038
Instability factor (IF)	1.15	1.00–1.31
Second harmonics (%)	35.7	
Postprandrial state		
Frequency (Hz)	0.051	0.045–0.057
Standard deviations (SD)	0.0032	0.0022–0.0040
Instability factor (IF)	1.14	1.00–1.34
Second harmonics (%)	71.4	
Power ratio (PR)	4.67	3.14–12.45

Table 6.5.2. Frequency dip parameters in duodenal ulcer patients.

		n = 14 median	range
F_{max}	(Hz)	0.053	0.045–0.058
F_{min}	(Hz)	0.037	0.035–0.042
T_{max}	(min)	11	7–13
T_{min}	(min)	3	1–4
T_d	(min)	8	5–11
T_s	(min)	5	3–7

6.5.4 Discussion

These data indicate that gastric myoelectrical behaviour recorded by means of cutaneous electrodes in patients with an untreated active duodenal ulcer is normal. In section 6.3 we described a group of 12 duodenal ulcer patients treated with a histamine-receptor antagonist. In these patients the myoelectrical behaviour was also indistinguishable from the control group. Despite the fact that there is some evidence for changes in gastric emptying rate in duodenal ulcer patients (35) our findings suggest that no major antral motor dysfunction is present in duodenal ulcer disease.

6.6 GASTRIC MYOELECTRICAL ACTIVITY DURING THE INFUSION OF CIS-DIAMMINEDICHLOROPLATINUM: AN ELECTROGASTROGRAPHIC STUDY

Co-authors E.J. van der Schee, T.A.W. Splinter, J.H.P. Wilson.

6.6.1 Abstract

Changes in gastric myoelectrical activity during the infusion of cis-diamminedichloroplatinum (cisplatin) were studied in 6 patients with a non-small cell bronchus carcinoma, by means of electrogastrography (EGG) using cutaneous electrodes. Before treatment all patients exhibited normal gastric myoelectrical behaviour. During the domperidone infusion normal interdigestive gastric myoelectrical activity was observed. During the cisplatin emetic phase, nausea and vomiting occurred in attacks lasting about 2 to 5 minutes. During an attack the gastric ECA frequency jumped to a higher level, remained at this level and then decreased abruptly, in most cases during nausea and vomiting, to the preexisting level.

It can be concluded that during the period of nausea and vomiting induced by cisplatin stimulation of the emetic centre, ECA frequency variations were observed that suggest disturbance of the control mechanism of the gastric pacemaker. It remains unclear whether these frequency abnormalities have a causal relation with the complaints or whether they are merely an associated phenomenon.

6.6.2 Introduction

Cis-diamminedichloroplatinum (II) (cisplatin) is one of the most effective antineoplastic agents in clinical use at present (1-3).

The drug, however, has severe gastrointestinal side effects, in particular nausea and vomiting, which are much more distressing than that of most other cytotoxic agents. The nausea and vomiting remain a major clinical problem, despite attempts to suppress the side effects by metoclopramide, domperidone, phenothiazines, cannabinoids, and corticosteroids (4-8).

Nausea and vomiting can occur as a result of stimuli that activate the emetic centre (9). Although these stimuli may be peripheral (upper gastrointestinal tract) or central (chemoreceptor trigger zone), most data (10,11) suggest that the emetic stimulus of cisplatin is centrally mediated. Antagonism of cisplatin-induced emesis by metoclopramide (4,5) and domperidone (5) suggests a dopaminergic component.

During vomiting the pattern of gastric motility changes markedly (9). Myoelectrical activity plays an important role in the control of gastric motor activity. The effects of cisplatin on gastric myoelectrical activity are therefore of potential interest as they may help increase our knowledge of the myoelectrical changes in the stomach, induced by stimulation of the emetic centre. The stomach has an inherent rhythmic myoelectrical activity with a repetition frequency of about 0.05 Hz, which is referred to as slow wave or electrical control activity (ECA) (12,13). In this study we use the term ECA. When motor activity is present, the ECA is accompanied by a second component, with or without superimposed fast oscillating potential changes (spikes or spike activity), in this study referred to as electrical response activity (ERA) (13).

With the development of electrogastrography (EGG) using skin electrodes it has become possible to examine gastric myoelectrical activity in a non-invasive fashion in both the fasting and postprandial states and so obtain information about the gastric ECA frequency, the presence of ERA and tachygastrias (14-23).

In view of our interest in electrogastrographic abnormalities in various disease states (24-26), and in particular in patients with nausea and vomiting, we decided to study patients undergoing intravenous infusion of cisplatin.

6.6.3 Methods

Subjects. Six male patients (mean age 61, range 56 - 67) participated in the study. All patients had a non-small cell, bronchus carcinoma. None had a history of any other gastrointestinal or systemic disorder. For all patients it was the first time that cisplatin had been administered. The treatment regime consisted of cisplatin 60 mg/m^2, administered over a 4 hour period. To reduce the intensity of the nausea and vomiting, domperidone (25 mg/hour) was given i.v. starting 4 hours before and continuing during the cisplatin infusion. We felt that it would be unethical to withdraw the domperidone for the purpose of the study.

Technique of recording. Gastric myoelectrical activity was recorded by means of cutaneous electrodes as described by Van der Schee et al (19), Smout et al (27) and Geldof et al (26,28,29).

Several days before treatment gastric myoelectrical activity during the fasting (30 min) and postprandial state (30 min) was recorded in all patients. A test meal, consisting of 250 ml of yoghurt with 20 g of sugar, was given and consumed within 4 min, while the recording was continued. The composition of the test meal was: 990 kJ, 8.75 g protein, 8.75 g fat and 30 g carbohydrate.

On the treatment day (after an overnight fast) the recording of the myoelectrical activity was started 60 min before the start of the cisplatin infusion (during domperidone i.v.) and was stopped 5 hours after the start of the cisplatin infusion. Patients continued to fast for the duration of the cisplatin infusion and several hours afterwards. They concomittantly received an infusion of L-glucose 5%.

Subjects lay quietly in a supine position during most of the recording session (only sitting up while taking the test meal or during vomiting).

Signal analysis. Signal analysis was performed using running spectrum analysis, based on a fast Fourier transform algorithm, as described by Van der Schee et al (19) and Geldof et al (26, 28,29). This procedure generates a series of overlapping spectra, called running spectra, which are plotted using grey-scale plots, giving time, frequency and power information simultaneously. Using this method frequency variations of 0.0039 Hz can be recognized (19). Tachygastrias with a duration of at least 64 s can be detected (19).

The mean gastric ECA frequency (Hz), its standard deviation (GFSD) and its power content could be computed for each period to be analysed e.g. the fasting or postprandial states. The GFSD was used as a measure of the stability of the gastric frequency over the period analysed. The larger the GFSD the more unstable the frequency.

Since the absolute value of the amplitude (mV) of a recorded cutaneous signal (and thus its power content, the amplitude being the square root of the power) is influenced by a number of factors (e.g. electrode-skin resistance, tissue conductivity, electrode distance from the stomach wall), it is impossible to make a comparison of inter-individual and even intra-individual power data (recorded in different sessions). Therefore in this study only power changes in the gastric ECA frequency observed during one single recording session were used for analysis.

A tachygastria was considered to be present if a frequency about 2.5 to 3.5 times higher than the normal gastric ECA frequency could be recognized in the spectra, while during this time period the normal gastric ECA frequency was absent. Where it was considered to be necessary, running spectrum analysis of the respiration signal was performed to exclude confusion between frequencies of respiratory origin and possible tachygastrias.

Statistical analysis. The Wilcoxon signed-rank test was used to evaluate whether a significant difference existed between the fasting myoelectrical behaviour before treatment and during domperidone infusion. Probability (p) values were derived from two-tailed tests with 0.05 being taken as the significant level.

The study was approved by the Medical Ethics Committee of the

Erasmus University, Rotterdam, on June 4, 1982 and carried out with the informed consent of the subjects.

6.6.4 Results

The results of the recordings taken in the fasting and postprandial states before the start of the treatment are summarized in table 6.6.1.

Table 6.6.1. EGG parameters for the 6 patients before the treatment regime in fasting and postprandial states.

Fasting state	
Gastric ECA frequency (Hz)	0.053 0.050–0.055
GFSD	0.0023 0.0019–0.0041
Postprandial state	
Gastric ECA frequency (Hz)	0.058 0.054–0.062
GFSD	0.0027 0.0020–0.0043
Postprandial state power increase	5.89 3.15–11.24

Values represent median and range.

In the fasting state a gastric ECA frequency of relatively low power was found with negligible frequency variations. Immediately after the test meal a dip in the ECA frequency was observed in all patients. The average frequency decrease was 16% of the fasting ECA frequency. After about 5 to 7 min the ECA frequency started to increase again, resulting in a temporary overshoot. After that the frequency, referred to as the postprandial ECA frequency, stabilized at a level which was equal to or somewhat higher than the fasting frequency. After the test meal a power increase in the gastric ECA was observed in all patients. The frequency and power/amplitude behaviour shown in fig. 6.6.1 is representative for these patients.

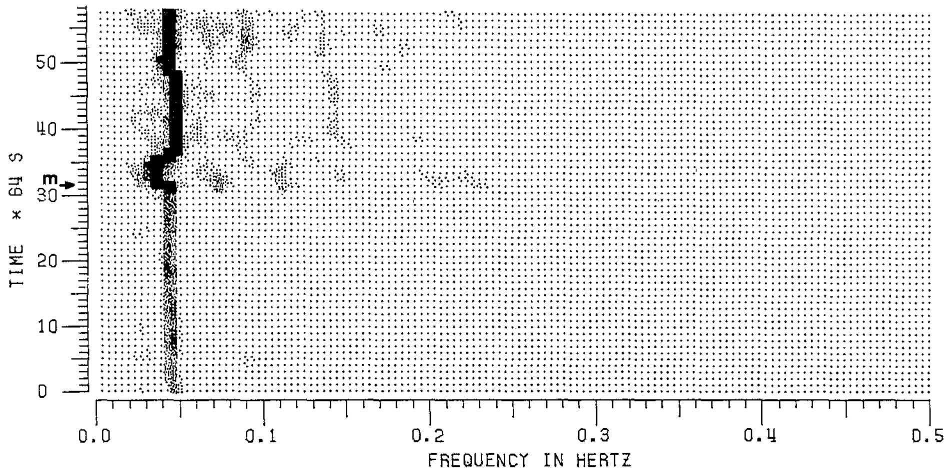


fig. 6.6.1 Grey-scale plot of the electrogastrogram of one of the patients before the treatment regime. The degree of blackness is proportional to the magnitude of the power of the electrogastrographic signal, divided into 36 distinct grey levels. Note the frequency dip and the subsequent power increase following the test meal, marked by 'M'.

The myoelectrical activity during the domperidone infusion was not significantly different from the fasting myoelectrical activity before the start of the treatment (table 6.6.1 and 6.6.2). Although the ECA frequency under domperidone tended to be somewhat lower, the difference was not significant. During the domperidone infusion small ECA frequency and power changes were seen, which were identical to the myoelectrical behaviour during the several phases of the interdigestive migrating complex (31).

In the first hours after the start of the cisplatin infusion no significant changes in myoelectrical behaviour were observed. The same small frequency and power changes were seen as during domperidone infusion and were similar to the phases of the interdigestive migrating complex illustrated in fig. 6.6.2 (29).

Table 6.6.2. EGG parameters for the 6 patients during domperidone infusion and during cisplatin/domperidone infusion.

Fasting	During Domperidone	During Domp./Cispl.
Gastric ECA frequency (Hz)	0.051 0.048–0.054	0.052 0.049–0.056 0.066* 0.062–0.074*
GFSD	0.0026 0.0022–0.0045	0.0025 0.0019–0.0034 0.0022* 0.0016–0.0038*
Power change during 'increased' frequency		1.39 0.96–2.05

Values represent median and range.
* Values for gastric ECA frequency and GFSD during periods of 'increased' frequency.

Despite the use of domperidone, all patients had attacks of nausea and vomiting which developed between 2 and 3 hours after starting the cisplatin infusion. During the cisplatin emetic phase, nausea and vomiting occurred in attacks of about 2 to 5 minutes. Between these attacks the patients were generally free of complaints. In the period that the attacks of nausea and vomiting occurred all 6 patients showed a remarkable ECA frequency behaviour. During an attack of nausea and vomiting the ECA frequency jumped to a higher level (median 0.066 Hz, range 0.062-0.074). The frequency, with negligible frequency variations, remained 10 to 35 minutes at this level to decrease abruptly, in most cases during vomiting, to the preexisting level. The power of the 'increased' ECA frequency was equal to the power of the gastric ECA frequency before the onset of the nausea, or somewhat higher, by up to a factor of 2.05. This characteristic frequency and power behaviour is illustrated in fig. 6.6.2.

Tachygastrias, defined as an ECA frequency 2.5 to 3.5 times higher than normal, were not observed.

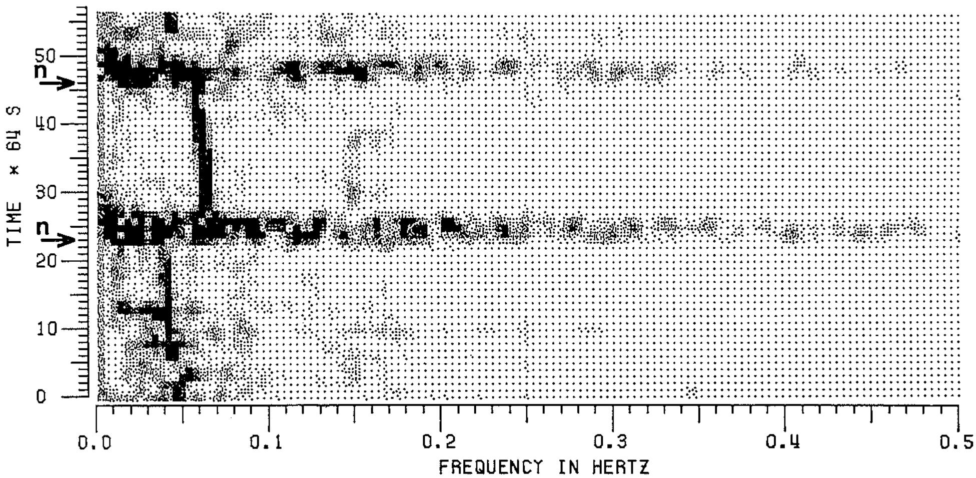


fig. 6.6.2 Grey-scale plot of the electrogastrogram of one of the patients during treatment with cisplatin and domperidone, with attacks of nausea and vomiting marked by 'N'. The frequency and power behaviour in this patient is characteristic. The pronounced frequency bands during the attacks of nausea and vomiting are motion artefacts. The frequency and power changes between 0 and 10 x 64 sec are characteristic for the change-over from phase II of the interdigestive migrating complex via phase III to phase I.

6.6.5 Discussion

The values for the fasting and postprandial gastric ECA frequency before the start of the treatment correspond to those reported in the literature for healthy subjects (12,15,19,26). There was thus no evidence that the patients studied had abnormal myoelectrical behaviour before starting the treament. Neither was there evidence that domperidone was responsible for the observed characteristic frequency and power behaviour during cisplatin infusion. In fact the small frequency and power changes found during domperidone infusion were identical to those described during the several phases of the interdigestive migrating complex (29), indicating that a normal interdigestive motor pattern was present.

The frequency abnormalities observed during the periods with nausea and vomiting probably reflect a disturbance in the control mechanism of the gastric pacemaker. We have observed the same type of frequency variations in patients with unexplained nausea and vomiting (24-26) and in gastric ulcer patients with nausea and vomiting (24,25).

In several disease states tachygastrias, i.e. frequencies 2.5 to 4 times the normal gastric ECA frequency are thought to be associated with nausea and vomiting (30-33). Tachygastrias, a term introduced by Code and Marlett (34), are thought to be generated in an ectopic focus which overrides the normal gastric pacemaker. In this study tachygastrias were not observed, although it should be realized that EGG has its limitations in detecting tachygastrias shorter than 64 seconds (19).

In conclusion, during the period of nausea and vomiting caused by stimulation of the emetic centre by cisplatin, ECA frequency variations were observed suggestive of a disturbance in the control mechanism of the gastric pacemaker. It remains unclear whether these frequency abnormalities have a causal relation with the complaints or whether they are merely an associated phenomenon.

6.6.6 References

1. Von Hoff D.D., Rozencweig M. Cis-diamminedichloroplatinum (II): a metal complex with significant anticancer activity. Adv. Pharmacol. Chemother. 1979; 16: 273-298.
2. Thigpen T., Shingleton H., Homesley H, et al. Cis-diamminedichloroplatinum (II) in the treatment of gynecologic maligancies: phase II trials by the Gynecologic Oncology Group. Cancer Treat. Rep. 1979; 63: 1549-1555.
3. Rozencweig M., Abele R., Von Hoff D.D., et al. Cisplatin: impact of a new anticancer agent on current therapeutic strategies. Anticancer Res. 1981; 1: 199-204.
4. Gralla R.J., Itri L.M., Pisko S.E., et al. Antiemetic efficacy of high dose metoclopramide: randomized trials with placebo and prochloroperazine in patients with chemotherapy-induced nausea and vomiting. N. Engl. J. Med. 1981; 305: 905-909.
5. Swann I.L., Thompson E.N., Qureshi K. Domperidone or metoclopramide in preventing chemotherapeutically induced nausea and vomiting. Br. Med. J. 1979; ii: 1188.
6. Yagoda A., Watson R.C., Gonzales-Vitale J.C., et al. Cis-diamminedichloroplatinum (II) in advanced bladder cancer. Cancer Treat. Rep. 1976; 60: 917-923.
7. Frytak S., Moertel C.G., O'Fallon J.R., et al. Delta-9-tetrahydrocannabinol as an antiemetic for patients receiving cancer chemotherapy. Ann. Intern. Med. 1979; 91: 825-830.
8. Aapro M.S., Alberts P.S. Dexamethasone as an antiemetic in patients treated with cisplatin. N. Engl. J. Med. 1981; 305: 520.
9. Borison H.L., Wang S.C. Physiology and pharmacology of vomiting. Pharmacol. Rev. 1953; 5: 193-230.
10. Wolf W.A., Manaka R.C. Synthesis and distribution of ^{195m}Pt Cis-diamminedichloroplatinum (II). J. Clin. Hematol. Oncol. 1976; 7: 79-95.
11. Higby D.J., Buchholtz L., Chary K., et al. Kinetics of cisplatinum (DDP) with intensive diuresis. Proc. Am. Assoc. Cancer Res. and ASCO 1977; 18: 110.

12. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.
13. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
14. Thouvenot J., Tonkovic S., Penaud J. Electrosplanchnography: Method for electrophysiological exploration of the digestive tract. Acta Med. Iugosl. 1973; 27: 227-247.
15. Brown B.H., Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.
16. Smallwood R.H., Brown B.H., Duthie H.L. An approach to the objective analysis of intestinal smooth muscle potentials recorded from surface electrodes. In: Vantrappen G., ed. Proc. 5th Int. Symposium on Gastrointestinal Motility, Leuven. Belgium. Typoff-Press, 1975: 248-253.
17. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. What is measured in electrogastrography? Dig. Dis. Sci. 1980; 25: 179-187.
18. Smout A.J.P.M., Van der Schee E.J., Grashuis J.L. Postprandial and interdigestive gastric electrical activity in the dog recorded by means of cutaneous electrodes. In: Christensen J., ed. Gastrointestinal motility. New York: Raven Press, 1980: 187-194.
19. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals recorded from dogs and man. In: Wienbeck M., ed. Motility of the digestive tract. New York: Raven Press, 1982: 241-250.
20. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.
21. Abell T., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in humans shown by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.
22. Hamilton J.W., Bellahsene B.E., Reichelderfer M., Webster J.G., Bass P. Human electrogastrograms, comparison of surface

and mucosal recordings. Dig. Dis. Sci. 1986; 31: 33-39.

23. Geldof H., Van der Schee E.J., Grashuis J.L. Accuracy and reliability of electrogastrography. (abstr.) Gastroenterology 1986; 90: 1425.

24. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Electrogastrographic findings in patients with nausea and vomiting. (abstr.) Gut 1983; 24: A476.

25. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Gastric dysrhythmia; an electrogastrographic study. (abstr.) Gastroenterology 1983; 84: 1163.

26. Geldof H., Van der Schee E.J., Van Blankenstein M., Grashuis J.L. Electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting. Gut 1986; 27: 799-808.

27. Geldof H., Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Electrogastrography. In: Akkermans L.M.A., Johnson A.G., Read N.W. eds. Gastric and gastroduodenal motility. New York: Praeger Publishers, 1984: 163-175.

28. Smout A.J.P.M., Van der Schee E.J., Akkermans L.M.A., Grashuis J.L. Recording of gastrointestinal activity from surface electrodes. Scand. J. of Gastroenterol. 1984; 19: suppl. 96: 11-18.

29. Geldof H., Van der Schee E.J., Grashuis J.L. Electrogastrographic characteristics of interdigestive migrating complex in humans. Am. J. Physiol. 1986; 250: G165-G171.

30. Telander R.L., Morgan K.G., Kreulen D.L., Schmalz P.F., Kelly K.A., Szurszewski J.H. Human gastric atony with tachygastria and gastric retention. Gastroenterology 1978; 75: 497-501.

31. You C.H., Lee K.Y., Chey W.Y., Menguy R. Electrogastrographic study of patients with unexplained nausea, bloating and vomiting. Gastroenterology 1980; 79: 311-314.

32. Reynolds R.P.E., Bardakjian B.L., Diamant N.E. A case of antral tachygastria: symptomatic and myoelectric improvement with gastroenterostomy and domperidone therapy. Can. Med. Assoc. J. 1983; 128: 826-829.

33. Chey W.J., You C.H., Lee K.Y. Menguy R. Gastric Dysrhythmia:

clinical aspects. In: Chey W.J. ed. Functional disorders of the digestive tract. New York: Raven Press, 1983: 175-181.

34. Code C.F., Marlett J.A. Canine tachygastria. Mayo Clin. Proc. 1974; 49: 325-332.

7. Summary and conclusions

The main aim of this thesis was to investigate whether electrogastrography (EGG), the recording of gastric myoelectrical activity by means of electrodes attached to the abdominal skin, can improve our understanding of gastric myoelectrical activity in disease.

The accuracy and reliability of EGG was studied by comparing cutaneous recordings with serosal recordings in a patient after laparotomy, and by performing repeat studies in healthy individuals. The fundamental frequency in the electrogastrogram in man was shown to be of gastric origin and equal to the repetition frequency of the gastric electrical control activity (ECA). The gastric ECA frequency can be measured reliable by EGG. The reliability of measurements of the postprandial amplitude increase of the gastric frequency by EGG (an indicator of gastric motor activity) can be improved by prolonging the fasting recording period but this does not seem to be necessary for clinical applications.

The influence of the interdigestive migrating complex, an important physiological phenomenon in the fasting state, on the electrogastrographic signal was studied by simultaneous measurements of gastric motility and EGG. We found that 1) in humans the gastric ECA frequency is less stable during the motor activity front of the interdigestive migrating complex than during motor quiescence; 2) the gastric frequency is lower during phase II motor activity than during motor quiescence; 3) the amplitude of the gastric frequency component in the electrogastrogram is correlated with motor activity, except during phase III; 4) a characteristic frequency and amplitude behaviour of the gastric component in the electrogastrogram during phase III can only be recognized in a minority of interdigestive migrating complexes; 5) electrogastrography cannot at present be used to identify precisely the different phases of the interdigestive migrating complex.

We subsequently tried to define the normal electrogastrogram. Gastric myoelectrical activity in healthy subjects in the fasting state was characterised by a stable gastric ECA frequency with a relatively small amplitude. Immediately after the test meal a frequency dip was observed in every subject. The average frequency decrease was about 20% of the fasting frequency. After about 5 minutes the gastric ECA frequency started to increase again, generally resulting in a small, temporary overshoot. After that the ECA frequency stabilised at a level which is at least equal to or somewhat higher than the fasting ECA frequency, with negligible frequency variations. The amplitude of the gastric ECA frequency increased in all subjects postprandially. Both the fasting and the postprandial ECA frequencies increased with age.

The control mechanisms of the postprandial motor- and myoelectrical behaviour are not clearly understood. We therefore studied the effects of sham- and 'tube-feeding' in healthy volunteers and the postprandial myoelectrical behaviour in patients undergoing gastric bypass surgery. We found that: 1) cephalic-vagal stimulation does not evoke postprandial antral phasic contractions and thus amplitude changes in the electrogastrogram; 2) the presence of food in the stomach is necessary for the induction of postprandial antral motor activity. It is likely that both hormonal and neural mechanisms are important in the control of gastric myoelectrical behaviour.

After defining the electrogastrographic characteristics of the gastric myoelectrical behaviour in healthy subjects several patients groups were studied.

The abnormal myoelectrical behaviour observed in patients with unexplained nausea and vomiting and in patients with an active gastric ulcer complicated by nausea and vomiting was almost identical and was characterised by: 1) instability of the gastric pacemaker frequency; 2) tachygastrias in both the fasting and postprandial states; 3) the absence of the normal amplitude increase in the postprandial electrogastrogram. This last characteristic was correlated with a delayed gastric emptying of solid food. Abnormal myoelectrical behaviour was not found in gastric ulcer patients without nausea and vomiting or in duodenal ulcer patients.

Highly selective vagotomy was, ten days after operation, associated with changes in the myoelectrical behaviour, in particular in the postprandial state, which were partly reversible after 6 months. This abnormal myoelectrical behaviour was characterised by: a) the absence of the normal postprandial amplitude increase of the gastric ECA frequency in the electrogastrogram, which could possibly reflect a temporary failure to convert the interdigestive motility pattern into a postprandial pattern; b) the absence of the normal postprandial initial dip in ECA frequency followed by an increase in ECA frequency to levels higher than fasting levels; c) tachygastrias. These changes were not observed in patients undergoing a cholecystectomy.

In 81% of patients with complaints of nausea and vomiting 1 to 6 years after highly selective vagotomy abnormal myoelectrical activity was observed, characterised by: a) the absence of the initial postprandial dip in gastric ECA frequency; b) the absence of the normal postprandial amplitude increase of the gastric ECA frequency in the electrogastrogram, which was correlated with a delayed gastric emptying for a solid meal; c) tachygastrias.

These results emphasize once more the importance of studying the myoelectrical activity in the postprandial state. The absence of the postprandial amplitude changes of the gastric ECA frequency in the electrogastrogram seems to be important with respect to complaints of nausea and vomiting in view of the observed correlation with a delayed gastric emptying for a solid test meal. The number of tachygastrias observed with EGG is much smaller than reported in the literature. This can partly be due to the fact that EGG has its limitations in the detection of tachygastrias shorter than 64 seconds. It is not known, however, to what extent the intraluminal mucosal suction electrodes, used in other studies, may give rise to tachygastrias, in particular in a diseased stomach.

Signal analysis by running spectrum analysis is a suitable technique to extract relevant information from the electrogastrogram. Running spectrum analysis provides time, frequency and amplitude information and has the additional important advantage of separating frequencies of respiratory origin from the gastric ECA frequency, which is often a problem with visual analysis.

Electrogastrography can thus be regarded as a powerful non-invasive tool for the study of gastric myoelectrical activity in both health and disease.

Samenvatting en conclusies

Electrogastrografie (EGG) is het registreren van de myoelectrische activiteit van de maag met behulp van buikhuid electroden. In dit proefschrift wordt het onderzoek beschreven naar de klinische toepasbaarheid van EGG.

Voordat EGG klinisch kan worden toegepast is het noodzakelijk de nauwkeurigheid en de betrouwbaarheid van de methode te toetsen. Uit het onderzoek blijkt dat 1) de grond frequentie van het electrogastrogram bij de mens afkomstig is van de maag en gelijk aan de herhalings frequentie van de "electrical control activity" (ECA); 2) EGG een betrouwbare weergave van de ECA frequentie , en van de frequentie variaties mogelijk maakt; 3) met de in deze studie gebruikte registratie tijd in nuchtere toestand (30 minuten) het meten van de postprandiale amplitude toename van de ECA frequentie minder betrouwbaar is ten gevolge van periodieke contractiele activiteit in de interdigestieve fase; 4) het verlengen van de registratie in de nuchtere toestand de betrouwbaarheid van het EGG wel doet toenemen maar dat langer registeren niet noodzakelijk is voor klinische toepassing.

In de nuchtere toestand treedt er in de maag periodiek contractiele activiteit op. De invloed van deze interdigestieve contractiele activiteit op het electrogastrogram werd onderzocht en tevens werd nagekeken of het mogelijk was de verschillende fasen van de interdigestieve contractiele activiteit van de maag te onderscheiden. Dit is belangrijk omdat de fasen (fase I: afwezige contractiele activiteit, fase II: onregelmatige contractiele activiteit, fase III: sterke regelmatige contractiele activiteit) belangrijke fysiologische markers zijn. Uit het onderzoek blijkt dat 1) bij de mens de ECA frequentie van de maag minder stabiel is tijdens contractiele activiteit dan in rust; 2) de maag frequentie lager is gedurende fase II contractiele activiteit dan bij afwezigheid van contractiele activiteit; 3) de amplitude van de ECA frequentie in het electrogastrogram gecorreleerd is met de sterkte van de contractiele activiteit, behalve tijdens fase III; 4) een karakteristiek frequentie en amplitude patroon van de ECA frequentie in het electrogastrogram gedurende fase III alleen gezien wordt in een minderheid van de interdigestieve cycli; 5) met EGG het niet mogelijk is de diverse fasen van de interdigestieve contractiele activiteit te onderscheiden zoals die gedefinieerd worden door manometrie.

De volgende logische stap is het definieren van de myoelectrische activiteit van de maag in een gezonde controle populatie. In nuchtere toestand is de ECA frequentie stabiel met een relatief kleine amplitude. Direct na een testmaaltijd wordt bij iedere proefpersoon een tijdelijke frequentie daling waargenomen. Ten opzichte van de ECA frequentie in nuchtere toestand bedraagt deze frequentie daling ongeveer 20%. Na 5 tot 10 minuten stijgt de frequentie kortdurend tot een iets hogere waarde dan in nuchtere toestand. Daarna stabiliseert de ECA frequentie zich op een niveau gelijk of iets hoger dan de ECA frequentie in nuchtere toestand, zonder noemenswaardige frequentie variaties. Na de testmaaltijd wordt in alle personen een toename van de amplitude gezien. Opmerkelijk is dat zowel de nuchtere alsook de postprandiale ECA frequentie toeneemt met de leeftijd.

De regel-mechanismen van het postprandiale myoelectrische gedrag zijn onvoldoende bekend. Uit een onderzoek naar de effecten van gesimuleerde- en sonde-voeding bij gezonde proefpersonen en het postprandiale myoelectrische gedrag in adipeuze patienten na een maag verkleinings operatie blijkt dat: 1) na cephale vagale stimulatie geen toename in amplitude wordt gezien en dus geen antrale contractiele activiteit; 2) de aanwezigheid van voedsel in de maag noodzakelijk is voor de inductie van postprandiale contractiele activiteit. Ten aanzien van het postprandiale frequentie gedrag kunnen geen conclusies worden getrokken, maar het is waarschijnlijk dat zowel hormonale alsmede neurale controle mechanismen belangrijk zijn.

Na het definieren van de electrogastrografische karakteristieken van de myoelectrische activiteit van de maag bij gezonde vrijwilligers zijn diverse patienten groepen bestudeerd.

Het abnormale myoelectrische gedrag waargenomen bij patienten met onbegrepen misselijkheid en braken en bij patienten met een ulcus ventriculi gecompliceerd door misselijkheid en braken, wordt gekenmerkt door 1) een instabiliteit van de ECA frequentie van maag; 2) tachygastrien in zowel nuchtere als postprandiale toestand; 3) de afwezigheid van de normale postprandiale amplitude toename van de ECA frequentie. Dit laatste is gecorreleerd met een vertraagde maag ontlediging van vast voedsel. Afwijkende myoelectrische activiteit wordt niet waargenomen bij patienten met een ulcus ventriculi zonder misselijkheid en braken of bij patienten met een ulcus duodeni.

Het onderzoek naar het myoelectrische gedrag bij patienten na een "highly selective vagotomy" (HSV) resulteert in de volgende bevindingen. Tien dagen na de vagotomie worden, m.n. in de postprandiale toestand, afwijkingen gezien in de myoelectrische activiteit. Deze abnormale myoelectrische activiteit, reversibel na 6 maanden, wordt gekenmerkt door: a) de afwezigheid van de normale postprandiale amplitude toename van de ECA frequentie in het electrogastrogram, hetgeen kan wijzen op een onvermogen het interdigestieve motoriek patroon om te schakelen in het postprandiale patroon; b) de afwezigheid van de initiele postprandiale frequentie daling en de daaropvolgende frequentie toename; c) tachygastrien. Het lijkt zeer waarschijnlijk dat deze veranderingen een gevolg zijn van de vagotomie omdat zij niet worden waargenomen bij patienten na een cholecystectomie.

Bij 81% van de patienten met misselijkheid en braken wordt 1 tot 6 jaar na een HSV abnormale myoelectrische activiteit waargenomen die gekenmerkt wordt door: a) de afwezigheid van de initiele postprandiale frequentie daling; b) de afwezigheid van de normale postprandiale amplitude toename, welke gecorreleerd is met een vertraagde maagontlediging van vast voedsel en c) tachygastrien.

Deze maatregelen benadrukken het belang de myoelectrische activiteit in de postprandiale toestand te bestuderen. Met name de afwezigheid van de postprandiale amplitude toename van de ECA frequentie in het electrogastrogram lijken gecorreleerd te zijn met een afwijkende maag motoriek. Het door ons met EGG waargenomen aantal tachygastrien is klein vergleken met de aantallen vermeld in de literatuur. Dit kan gedeeltelijk verklaard worden door het feit dat EGG zijn beperkingen heeft in het detecteren van tachygastrien korter dan 64 seconden. Het is echter onbekend in welke mate een intraluminale zuigelectrode, zoals gebruikt in de meeste studies, aanleiding geeft tot het ontstaan van tachygastrien, met name in een zieke maag.

Uit ons onderzoek blijkt dat running spectrum analysis als signaal analytische methode geschikt is om relevante informatie uit het electrogastrogram te extraheren. Running spectrum analysis verschaft ons tegelijkertijd informatie over frequentie en amplitude in het verloop van de tijd. Voorts is het vermogen frequenties van respiratoire origine te scheiden van de ECA frequentie, vaak een probleem met visuele inspectie, een belangrijk voordeel van deze methode.

Electrogastrografie kan beschouwd worden als een goede methode om de myoelectrische activiteit van de maag te bestuderen, zowel bij gezonden als bij patienten.

References

1. Abell T.L., Tucker R., Malagelada J-R. Feasibility of simultaneous external and mucosal electrogastrogram in man. (abstr) Gastroenterology 1983; 84: 1085.
2. Abell T., Malagelada J-R. Glucagon-evoked gastric dysrhythmias in humans showed by an improved electrogastrographic technique. Gastroenterology 1985; 88: 1932-1940.
3. Alvarez W.C. The electrogastrogram and what it shows. JAMA 1922; 78: 1116-1119.
4. Andrews P.L.R., Grundy D., Scratcherd T. Reflex excitation of antral motility induced by gastric distension in the ferret. J. Physiol. 1980; 298: 79-84.
5. Andrews P.L.R., Scratcherd T. The gastric motility patterns induced by direct and reflex excitation of the vagus nerves in the anesthetized ferret. J. Physiol 1980; 302: 363-378.
6. Atanassova E., Papasova M. Gastrointestinal motility. In: Crane R.K., ed. Gastrointestinal Physiology II, vol. 12. Baltimore, University Park Press, 1977: 35-69.
7. Blackman R.B., Tuckey J.W. The measurement of power spectra. Dover Publications Inc. New York, 1958.
8. Brown B.H., Smallwood R.H., Duthie H.L., Stoddard C.J. Intestinal smooth muscle electrical potentials recorded from surface electrodes. Med. Biol. Eng. 1975; 13: 97-103.
9. Code C.F., Schlegel J.F. The gastrointestinal interdigestive housekeeper: motor correlates of the interdigestive myoelectric complex in the dog. In: Daniel E.E., ed. Proc. of the 4th Int. Symposium on Gastrointestinal Hormones. 1973: 631-634.
10. Code C.F., Marlett J.A. The interdigestive myoelectrical complex of the stomach and small bowel of dogs. J. Physiol. 1975; 246: 289-309.
11. Crowe R., Burnstock G. Comparitive studies of quinacrine-positive neurones in the myenteric plexus of

stomach and intestine of guinea pig and rat. Cell and Tissue Research 1981; 221: 93-107.

12. Davis R.C., Garafolo L., Gault F.P. An exploration of abdominal potentials. J. Comp. Physiological Psychology 1957; 50: 519-523.
13. Davis R.C., Garafolo L., Kveim K. Conditions associated with gastrointestinal activity. J. Comp. Physiological Psychology 1959; 52: 466-475.
14. Duthie H.L., Kwong N.K., Brown B.H., Whittaker G.E. Pacesetter potential of the human gastroduodenal junction. Gut 1971; 12: 250-256.
15. Edin R., Lundberg J., Terenius L., Dahlstrom A., Hokfelt T., Kewenter J., Ahlman H. Evidence for vagal enkephalinergic neural control of the feline pylorus and stomach. Gastroenterology 1980; 78: 492-497.
16. El-Sharkawy T.Y., Morgan K.G., Szurszewski J.H. Intracellular activity of canine and human gastric muscle. J. Physiol 1978; 279: 291-307.
17. Furness J.B., Costa M. Projections of intestinal neurones showing immunoreactivity for vasoactive intestinal polypeptide are consitent with these neurones being the inhibitory neurones. Neuroscience Letters 1979; 15: 199-205.
18. Gabella G. Structure of muscle and nerves in the gastrointestinal tract. In: Johnson L.R., ed. Physiology of the Gastrointestinal Tract. New York: Raven Press, 1981: 197-241.
19. Geddes L.A. Electrodes and the measurement of bioelectric events. Wiley Interscience, New York, 1972.
20. Geldof H., van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Electrogastrography. In: Akkermans L.M.A., Johnson A.G., Read N.W. eds. Gastric and Gastroduodenal Motility. New York: Praeger Publishers, 1984: 163-175.
21. Grundy D., Scratcherd T. The role of the vagus and sympathetic nerves in the control of gastric motility. In: Akkermans L.M.A., Johnson A.G., Read N.W. eds. Gastric and Gastroduodenal Motility. New York: Praeger Publishers, 1984: 21-33.

22. Hamilton J.W., Bellahsene B.E., Reichelderfer M., Webster J.G., Bass P. Human cutaneous electrogastrography (EGG). Comparison with internal recordings. (abstr) Gastroenterology 1983; 84: 1180.
23. Hinder R.A., Kelly K.A. Human gastric pacesetter potential. Site of origin, spread and response to gastric transsection and proximal gastric vagotomy. Am. J. Surg. 1977; 133: 29-33.
24. Hoyes A.D., Sikri K.L., Barber P. Localization of substance P-like Immunoreactivity in the intraluminal nerve plexuses of the guinea-pig stomach using immunofluorescence and immunoperoxidase techniques. J. Anatomy 1982; 135: 319-332.
25. Hunt J.N., Spurrell W.R. The pattern of emptying of the human stomach. J. Physiol. 1951; 113: 157-168.
26. Hunt J.N., Stubbs D.F. The volume and energy content of meals as determinants of gastric emptying. J. Physiol. 1975; 215: 209-225.
27. Ingram P.W., Richards D.L. Observations of potential differences of the human stomach by a new electrode and measuring system. Gastroenterology 1953; 25: 273-289.
28. Itoh Z., Aizawa I., Takeuchi S., Takayanagi R. Diurnal changes in gastric motor activity in conscious dogs. Am. J. Dig. Dis. 1977; 22: 117-124.
29. Jahnberg T., Abrahamsson H., Jansson G., Martinson J. Gastric relaxatory response to feeding before and after vagotomy. Scan. J. Gastroenterol. 1977; 12: 225-228.
30. Kelly K.A., Code C.F., Elveback L.R. Patterns of canine gastric electrical activity. Am. J. Physiol. 1969; 217: 461-470.
31. Kelly K.A. Motility of the stomach and gastroduodenal junction. In: Johnson L.R., ed. Physiology of the gastrointestinal tract. New York: Raven Press, 1981: 393-410.
32. Krasil'nikov L.G. Linicheskope Znochenize elektrogastrogrefil. [Clinical importance of electrogastrography.] Soviet Medicine 1960; 24: 107-114.
33. Linkens D.A., Cannell A.E. Interactive graphic analysis of gastrointestinal electrical signals. IEEE Trans. Biomed. Eng. 1974; 21: 335-339.

34. Lux G., Lederer P., Femppel J., Rosch W., Domschke W. Spontaneous and 13-NLE-motilin induced interdigestive motor activity of oesophagus, stomach and small intestine in man. In Christensen J., ed. Gastrointestinal Motility. New York: Raven Press, 1980: 269-278.
35. Maddern G.J., Horowitz M., Hetzel D.J., Jamieson G.G. Altered solid and liquid gastric emptying in patients with duodenal ulcer disease. Gut 1985; 26: 689-693.
36. Martin A., Thouvenot J., Touron P. Variations periodiques des potentiels cutanes abdominaux en relation avec l'activite digestive. C. R. Soc. Biol. 1967; 161: 2595-2600.
37. Martin A., Thouvenot J., Masson J-M., Touron P. Interet et place de l'electrosplanchnografie en pathologie psychosomatique digestive. Ann. Med.-Psychol. 1970; 128: 31-41.
38. Martin A., Thillier J.L. L'electrogastroenterographie (EGEG). C. R. Soc. Biol. 1971; 165: 1727-1733.
39. Martin A., Thillier J.L. Un viscere digestif en activite, possede-t-il un axe electrique? C. R. Soc. Biol. 1971; 165: 1704-1711.
40. Martin A., Thillier J.L. La vectorgastrogramme. Moyen de comprehension et de validation de l'electrogastroenterographie. Nouv. Presse Med. 1972; 1: 453-456.
41. Martin A., Thillier J.L., Moline J. Effects de la section du vague sur la motricite gastrique chez l'homme. Etude electrogastroenterographique. J. Physiol. (Paris) 1972; 65: 145A.
42. Meyer J.H., Thomson J.B., Jehn D., Thomas J.B. Size of liver particles emptied from the human stomach. Gastroenterology 1981; 80: 1489-1496.
43. Mirizzi N., Scafoglieri U. Optimal directions of the electrogastrographic signal in man. Med. Biol. Eng. Comp. 1983; 21: 385-389.
44. Moore J.D., McIntyre B., Alazraki N. Gastric emptying of combined liquid-solid meals in healed duodenal ulcer. Dig. Dis. Sci. 1985; 30: 1134-1138.

45. Nelson T.S., Kohatsu S. Clinical electrogastrography and its relation to gastric surgery. Am. J. Surg. 1968; 116: 215-222.
46. Nishioka T., Sekiguchi T., Kogura M., Kusano M., Arai H., Katoh R., Okamura S., Matsuzaki T., Fukazawa T., Akiyama T., Ohwada H., Kobayashi S. A study on continuous simultaneous recordings of gastrointestinal motility and intraluminal pH in human healthy subjects. Jap. J. Gastroenterol. 1981; 78: 2065-2073.
47. Paintal A.S. A study of gastric stretch receptors. Their role in the peripheral mechanism of satiation of hunger and thirst. J. Physiol 1954; 126: 255-270.
48. Peeters T.L., Vantrappen G.R., Janssens J. Control of gut motility. In: Bloom S.R., Polak J.M., Lindenlaub E. eds. Systemic Role of Regulatory Peptides. Stuttgart-New York, FK Schattauer Verlag, 1982: 195-208.
49. Prove J., Ehrlein H-J. Motor function of gastric antrum and pylorus for evacuation of low and high viscosity meals in dogs. Gut 1982; 23: 150-156.
50. Ruckebusch Y., Bueno L. The effect of feeding on the motility of the stomach and the small intestine in pig. Brit. J. Nutrition 1976; 35: 397-405.
51. Sarna S.K. Gastrointestinal electrical activity; terminology. Gastroenterology 1975; 68: 1631-1635.
52. Smallwood R.H., Brown B.H., Duthie H.L. An approach to the objective analysis of intestinal smooth muscle potentials recorded from surface electrodes. In: Vantrappen G., ed. Proc. 5th Int. Symposium on Gastrointestinal Motility, Leuven. Belgium. Typoff-Press, 1975: 248-253.
53. Smallwood R.H. Gastrointestinal electrical activity from surface electrodes. Thesis, Sheffield, England, 1976.
54. Smallwood R.H. Analysis of gastric electrical signals from surface electrodes using phase-lock techniques. Part 1 - System design. Med. Biol. Eng. Comput. 1978; 16: 507-512.
55. Smallwood R.H. Analysis of gastric electrical signals from surface electrodes using phase-lock techniques. Part 2 - System performance with gastric signals. Med. Biol. Eng. Comput. 1978; 16: 513-518.

56. Smout A.J.P.M. Myoelectrical activity of the stomach: gastroelectromyography and electrogastrography. Thesis, Erasmus University, Rotterdam, 1980.
57. Smout A.J.P.M., van der Schee E.J., Grashuis J.L. What is measured in electrogastrography? Dig. Dis. Sci. 1980; 25: 179-187.
58. Smout A.J.P.M., van der Schee E.J., Grashuis J.L. Postprandial and interdigestive gastric electrical activity in the dog recorded by means of cutaneous electrodes. In: Christensen J., ed. Gastrointestinal Motility. New York: Raven Press, 1980: 187-194.
59. Smout A.J.P.M., Van der Schee E.J., Akkermans L.M.A., Grashuis J.L. Recording of gastrointestinal activity from surface electrodes. Scan. J. Gastroenterol. 1984; 19: suppl. 96: 11-18.
60. Sobakin M., Mishin L.N. Novyye dannyyee metodiki I tekhaiki elektrogastrografll. [New data, methods, and techniques in electrogastrography.] In: Materialy po obmenu opytom I nauchymi dostizheniyami v meditsinskoy promyshlennosti, Moscow, 1958.
61. Sobakin M.A., Smirnov I.P., Mishin L.N. Electrogastrography. IRE Trans Bio. Med. Electron. 1962; 9:129-132.
62. Stern R.M. Effects of variation in visual and auditory stimulation on gastrointestinal motility. Psychological Reports 1964; 14: 799-802.
63. Stern R.M. Effects of contrast in stimulation on gastrointestinal motility. Psychological Reports 1965; 16: 156-158.
64. Stern R.M. A re-examination of the effects of response-contingent aversive tones on gastrointestinal activity. Psychophysiology 1966; 2: 217-223.
65. Stern R.M., Crawford H.E., Steward W.R., Koch K.L. Gastric myoelectrical activity in response to sham feeding in healthy human subjects. (abstr.) Gastroenterology 1985; 88: 1600.
66. Szurszewski J.H. A migrating electrical complex of the canine small intestine. Am. J. Physiol. 1969; 217: 1757-1763.
67. Szurszewski J.H. Modulation of smooth muscle by nervous

activity: a review and hypothesis. Federation Proceedings 1977; 36: 2456-2461.

68. Szurszewski J.H. Electrical basis for gastrointestinal motility. In: Johnson L.R., ed. Physiology of the Gastrointestinal Tract. New York: Raven Press, 1981: 1435-1466.

69. Thompson D.G., Richelson E., Malagelada J-R. Pertubation of gastric emptying and duodenal motility through the central nervous system. Gastroenterology 1982; 83: 1200-1206.

70. Thouvenot J., Tonkovic S., Penaud J. Electrosplanchnography: Method for electrophysiological exploration of the digestive tract. Acta. Med. Iugosl. 1973; 27: 227-247.

71. Tieman F., Reichertz P. Uber das Intestinale Elektrogastrogramm (EIG) und seine Bedeutung fur die Klinik. Medizinische Klinik 1959; 54: 654-668.

72. Tieman F., Reichertz P. Experimentelle Grundlagen des Elektro-Intestinogramms. Medicina Experimentalis 1959; 1: 17-26.

73. Tumpeer I.H., Blitzsten P.W. Registration of peristalsis by the Einthoven galvanometer. Am. J. Dis. Chil. 1926; 31: 454-455.

74. Tumpeer I.H., Phillips B. Hyperperistaltic electrographic effects. Am. J. Dis. Chil. 1932; 184: 831-836.

75. Van der Schee E.J., Smout A.J.P.M., Grashuis J.L. Application of running spectrum analysis to electrogastrographic signals recorded from dogs and man. In: Wienbeck M., ed. Motility of the Digestive Tract. New York: Raven Press, 1982: 241-250.

76. Van der Schee E.J. Electrogastrography, signal analytical aspects and interpretation. Thesis, Erasmus University, Rotterdam, 1984.

77. Vantrappen G., Janssens J., Hellemans J., Christofides N., Bloom S. Studies on the interdigestive (migrating) motor complex in man. In: Duthie H.L., ed. Gastrointestinal Motility in Health and Disease. Lancaster: MTP Press, 1977: 3-8.

78. Vantrappen G., Janssens J., Hellemans J., Ghoos Y. Interdigestive motor complex of normal subjects and patients

with bacterial overgrowth of the small intestine. J. Clin. Invest. 1977; 59: 1158-1166.

79. Vantrappen G., Janssens J., Peeters T.L. The migrating motor complex. Med. Clin. North Am. 1981; 65: 1311-1329.

80. Volkers A.C.W., Van der Schee E.J., Grashuis J.L. Electrogastrography in the dog: waveform analysis by a coherent averaging technique. Med. Biol. Eng. Comp. 1983; 21: 56-64.

81. Weber J., Kohatsu S. Pacemaker localization and electrical conduction patterns in the canine stomach. Gastroenterology 1970; 59: 717-726.

82. Weisbrodt N.W., Wiley J.N., Overholt B.F., Bass P. A relation between gastroduodenal muscle contractions and gastric emptying. Gut 1969; 10: 543-548.

83. Weisbrodt N.W. Gastric motility. In: Johnson L.R., ed. Gastrointestinal Physiology. St Louis, Mosby, 1981: 22-29.

84. Weisbrodt N.W. Motility of the small intestine. In: Johnson L.R., ed. Physiology of the Gastrointestinal Tract. New York: Raven Press, 1981: 411-444.

85. Weisbrodt N.W. Basic control mechanisms. In: Akkermans L.M.A., Johnson A.G., Read N.W. eds. Gastric and Gastroduodenal Motility. New York: Praeger Publishers, 1984: 3-20.

Verantwoording

Dit proefschrift werd bewerkt op de afdeling Interne Geneeskunde II en op de afdeling Medische Technologie van de Erasmus Universiteit. Velen hebben bijgedragen aan de totstandkoming ervan, waaronder in het bijzonder de staf en medewerkers van beide afdelingen. Enkelen wil ik afzonderlijk noemen. Prof. dr. M. Frenkel, destijds hoofd van Interne Geneeskunde II en mijn opleider, stimuleerde mij dit onderzoek te starten. Prof. J.H.P. Wilson, heeft als promotor in belangrijke mate bijgedragen aan het totstandkomen van dit proefschrift. Drs. M. van Blankenstein, een stuwende kracht achter het onderzoek en leverancier van vele "interessante" patienten. Van Dr. J.P. van de Merwe heb ik geleerd hoe statistiek behoort te worden gebruikt. Allen ben ik zeer erkentelijk. De samenwerking met de preklinische afdeling in de personen van dr. ir. E.J. van der Schee en dr. ir. J.L. Grashuis heb ik als zeer leerzaam en boeiend ervaren. Evert is in de laatste fase van het onderzoek en het schrijven van de artikelen en het proefschrift onmisbaar gebleken, niet in het minst door zijn hardnekkige optimisme. De medewerkers van de afdeling Maag-, Darm- en Leverziekten AMC Amsterdam en de collegae van het Bergweg Ziekenhuis ben ik dank verschuldigd voor het begrip dat ze konden opbrengen voor het feit dat het schrijven van een proefschrift tijd kost. Tenslotte wil ik Prof. dr. ir. C.J. Snijders, Prof. dr. G.N.J. Tijtgat en Prof. Dr. Bruining danken voor hun bereidwilligheid om, naast Prof. J.H.P. Wilson, deel uit te maken van de beoordelingskomissie.

De druk van dit proefschrift werd mede mogelijk gemaakt door financiele steun van Duphar Nederland B.V., Glaxo B.V., Janssen Pharmaceutica B.V. en Smith Kline & French B.V.

Curriculum vitae

De schrijver van dit proefschrift werd geboren op 9 augustus 1951 te Middelburg. Na het behalen van het diploma HBS-B aan de Stedelijke Scholengemeenschap te Middelburg in 1969 gestart met de opleiding tot vliegtuigbouwkundig ingenieur. In 1971, na het het tweede studiejaar te hebben afgerond, werd deze studie afgebroken en een aanvang gemaakt met de studie in de Geneeskunde aan de Gemeentelijke Universiteit te Amsterdam, alwaar in 1976 het Doctoraal-examen (cum laude) en in 1979 het Arts-examen werd afgelegd. Op 1 september 1979 werd de opleiding tot internist aangevangen in het Academisch Ziekenhuis Rotterdam, Dijkzigt, onder leiding van Prof. dr. M. Frenkel. Op 1 oktober 1984 werd hij als internist ingeschreven in het Specialisten Register. Vanaf 1 oktober 1984 tot 1 juli 1986 was hij werkzaam op de afdeling Maag-, Darm- en Leverziekten, hoofd Prof. dr. G.N.J. Tijtgat, van het Academisch Medisch Centrum te Amsterdam. Sinds 1 juli 1986 is hij als internist verbonden aan het Bergwegziekenhuis te Rotterdam.