

# Impaired Postprandial Gastric Slow Waves in Patients with Functional Dyspepsia

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The aim of this study was to investigate gastric myoelectrical activity in patients with functional dyspepsia. Thirteen healthy subjects and 14 patients with functional dyspepsia participated in the study. The electrogastrogram (EGG) recording was made in each subject for 30 min in the fasting state and 120 min after a standard test meal of 475 calories. Spectral analysis methods were applied to derive quantitative EGG parameters. There was no difference in the EGG between the patients and controls in the fasting state. However, abnormalities in the postprandial EGG were found in the patients. The percentage of 2–4 cpm waves was significantly lower ( $74.4 \pm 4.0\%$  vs  $85.7 \pm 1.6\%$ ,  $P < 0.03$ ) and the postprandial increase in EGG dominant power was significantly less ( $-0.52 \pm 0.92$  dB vs  $2.24 \pm 0.88$  dB,  $P < 0.03$ ) in patients than in controls. It was also found that the percentage of postprandial 2–4 cpm waves could be used to differentiate the patients with functional dyspepsia from the healthy controls with a specificity of 100% and a sensitivity of 43%. It was concluded that a subset of patients with functional dyspepsia have impaired gastric myoelectrical activity in the fed state.

**KEY WORDS:** electrogastrography; gastrointestinal motility; functional dyspepsia; gastric emptying.

Functional dyspepsia is a common clinical syndrome and its pathophysiology is not clearly known (1). A number of investigators have attempted to subdivide functional dyspepsia into three categories: dysmotility-like, ulcerlike, and refluxlike dyspepsia (2). This classification is based on symptoms and does not explain the underlying pathophysiological mechanism of functional dyspepsia. Gastrointestinal motor disorders have been found in patients with functional dyspepsia, such as gastric hypomotility and uncoordinated antral duodenal contractions (3–7).

Gastric motility is regulated by gastric myoelectrical activity. Previous studies have shown that abnormal gastric myoelectrical activities are associated with

gastric motility disorders and gastrointestinal symptoms such as nausea and vomiting (8–13), which are very common in functional dyspepsia. There are indications that gastric motor disorders in patients may be pathophysiologically attributed to gastric myoelectrical dysrhythmias (13–16). Abnormal gastric myoelectrical activity has been recently reported in children with functional dyspepsia (5, 17). Few studies have investigated gastric myoelectrical activity in adult patients with functional dyspepsia (13, 18). Geldof et al reported no difference between the patients and healthy controls in the EGG parameters they analyzed (12). No quantitative assessment of the regularity of gastric slow waves was performed, however, and the postprandial state was studied after a relatively small test meal (275 kcal).

EGG is an accurate measurement of the gastric slow wave (19–22) and is a noninvasive method for gastric myoelectrical activity. The frequency of gastric slow waves is measured in the EGG, whereas the contraction-related spike/second potentials are re-

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flected in the EGG as an increase in amplitude (20, 23). Numerous studies have used this technique to detect gastric motility disorders (14–16, 24–32).

The objective of this study was to investigate gastric myoelectrical activity in patients with functional dyspepsia using the EGG method.

## MATERIALS AND METHODS

### Subjects

The study was performed on 13 healthy controls without any gastrointestinal symptoms (6 men, 7 women, age: 23–41 years, mean: 31 years) and 14 patients with functional dyspepsia (4 men, 10 women, age: 26–66 years, mean: 44 years). All patients were clinically confirmed by negative endoscopy within three months prior to the study to have no mechanical obstructions or organic diseases. None of the patients had been diagnosed for gastroesophageal reflux, chronic intestinal pseudoobstruction, irritable bowel syndrome, or diabetes, and none had clinical biochemical and ultrasonographic evidence of any known organic disease. Patients with a history of gastrointestinal surgery or concomitant medication including prokinetic agents, anticholinergic agents, and calcium-channel blockers were excluded from the study. All patients had a history of dyspeptic symptoms of at least six months duration (continuous or intermittent). The following symptoms were evaluated: nausea, vomiting, anorexia, early satiety, postprandial bloating or distension, upper abdominal discomfort or pain, and belching. The symptoms were graded from 0 to 3 (0: absent; 1: mild; 2: moderate; 3: severe). A total score of  $\geq 6$  was required for the enrollment into the study.

All subjects were fasted for more than 6 hr prior to the study and had taken no medications with a known effect on gastrointestinal motility during the three days prior to the study. The study was approved by the Institutional Review Board at Integris Baptist Medical Center. Written consent was obtained from the subjects prior to the study.

### Electrogastrogram

Surface electrogastronomy was applied to record gastric myoelectrical activity. Before the placement of electrodes, the abdominal skin at the recording sites was cleaned with sandy skin-prep jelly (Omni Prep, Weaver & Co., Aurora, Colorado) to reduce impedance. The skin was rubbed until it was pinkish. Hair, if present, was shaved. Three Ag–AgCl ECG electrodes (Red Dot, 3M Health Care, St. Paul, Minnesota) were placed on the abdomen. Electrode 1 was placed at the midpoint between the xiphoid and the navel; electrode 2 was placed 5 cm to the left and 3 cm above this point; a reference electrode was placed in the lower quadrant near the left costal margin. The bipolar EGG signal was derived from electrodes 1 and 2 and amplified using a portable EGG recorder (Digitrapper EGG, Medtronic-Synectics Medical, Inc., Shoreview, Minnesota) with low and high cutoff frequencies of 1 and 18 cpm, respectively. Online digitization with a sampling frequency of 1 Hz was performed using an analog-to-digital converter installed on the recorder.

After a fast of more than 6 hr, the EGG recording was made in each subject for 30 min in the fasting state and 120 min after a standard test meal of turkey sandwich (475 calories; fat 32.4%, protein 17.5%, carbohydrate 50.1%). The study was performed with the subject in a supine position. The subject was asked to remain as still as possible during the entire recording period. Talking or reading was not permitted. The subject was allowed to watch regular TV programs and not allowed to fall asleep.

### Data Analysis

At the end of the study, the EGG data stored on the recorder were downloaded to an IBM 486 personal computer and subjected to computerized spectral analyses using the programs previously developed in our laboratory (33). Motion artifacts were visually identified and deleted before analysis. This was done by a laboratory technician who did not know the design and aim of the study. The technician was trained using EGG data obtained in a previous experiment in which 10 healthy subjects were asked to mimic various motions. The following parameters were computed from the EGG using the spectral analysis methods:

*Percentage of Normal 2–4 cpm Slow Waves.* The percentage of normal 2–4 cpm gastric slow waves, which reflects the regularity of gastric myoelectrical activity, was defined as the percent of time during which normal 2–4 cpm slow waves were present over the entire observation period. It was computed using the adaptive running spectral analysis method (33). Each EGG recording was divided into blocks of 1 min without overlapping. The power spectrum of each 1-min EGG was calculated and examined to see if the peak power was within the range of 2–4 cpm. The 1-min EGG was categorized normal if the dominant power was within the 2–4 cpm range. Otherwise, it was categorized as dysrhythmia.

*Percentage of Dysrhythmias.* The percentage of gastric dysrhythmias was defined as the percent of time during which dysrhythmias were present over the entire observation period. It was computed using the same method as previously stated. Gastric dysrhythmias include tachygastria, bradygastria, and arrhythmia. If the peak power of the 1-min EGG block was within the range of 0.5–2 cpm, the 1-min EGG was categorized bradygastria; if the peak power was within the range of 4–9 cpm, it was categorized tachygastria. The 1-min EGG was defined as arrhythmia if its power spectrum showed no dominant peak in the range of 0.5–9 cpm.

*EGG Dominant Frequency and Power.* The frequency at which the power spectrum of an entire EGG recording (30 min in the fasting state or 120 min in the fed state) had a peak power in the range of 0.5–9.0 cpm was defined as the EGG dominant frequency. The dominant frequency of the EGG has been shown to be equal to the frequency of the gastric slow wave measured from implanted serosal electrodes (22). It was computed using the smoothed power spectral analysis method (33).

The power at the dominant frequency in the power spectrum of the EGG was defined as the EGG dominant power. Previous studies (20, 33) have shown that the relative change of the EGG dominant power reflects gastric contractility. Decibel (dB) units were used to represent the

TABLE 1. EGG AS A PREDICTOR

	Patients	Healthy controls
Abnormal EGG	A	B
Normal EGG	C	D

power of the EGG. Assuming a sinusoidal signal with an amplitude of  $A$ , power ( $P$ ) in dB was expressed as  $P(\text{dB}) = 10 \times \log_{10}(A^2)$ .

**Change of EGG Dominant Power.** The change of EGG dominant power ( $\delta P$ ) was defined as the difference between the EGG dominant powers after and before the test meal.

**Instability Coefficient of Dominant Frequency.** The instability coefficient (IC) of the dominant frequency was defined as the standard deviation (SD) divided by the mean value of the dominant frequencies computed from 1-min EGG data blocks using the adaptive spectral analysis methods (33). It reflects the variation of the dominant frequency through the whole recording period.

**Abnormality of EGG Parameters in Fasting and Fed States.** A  $2 \times 2$  contingent table (Table 1) was used to investigate whether a particular EGG parameter could be used to predict functional dyspepsia. Definitions are as follows: sensitivity =  $A/(A + C)$ ; specificity =  $D/(B + D)$ ; negative predictive value =  $D/(C + D)$ ; and positive predictive value =  $A/(A + B)$ .

The normality of the EGG rhythmicity was defined as the mean value of the percentage of 2–4 cpm slow waves in fasting state in the healthy controls minus one standard error. The EGG recording was defined as abnormal in rhythmicity if its percentage of 2–4 cpm slow waves was below this value. The abnormality of EGG dominant power in response to the test meal was defined as a decrease in power at the dominant frequency after the test meal. The normality of the IC was defined as the mean value of the IC plus one standard error. The EGG recording was defined as abnormal in IC if its value was larger than this value. This definition is to ensure the biggest variation of the EGG dominant frequency.

### Statistical Analysis

All data were presented as mean  $\pm$  SEM. Student's  $t$  test and chi-square test were used to investigate the difference of the EGG parameters between the patients and the controls. A finding of  $P < 0.05$  was considered to be significant.

## RESULTS

In the fasting state, there was no significant difference in the percentage of 2–4 cpm slow waves between the patients and controls. The controls had a mean percentage of 2–4 cpm slow waves of  $79.5 \pm 4.0\%$  and the patients had a mean percentage of 2–4 cpm slow waves of  $71.1 \pm 6.7\%$  ( $P > 0.05$ ).

Abnormalities were found in the postprandial EGG in patients with functional dyspepsia. The total percent dysrhythmia was higher in the patients than in the controls ( $25.6 \pm 4.0\%$  vs  $14.3 \pm 1.6\%$ ,  $P <$

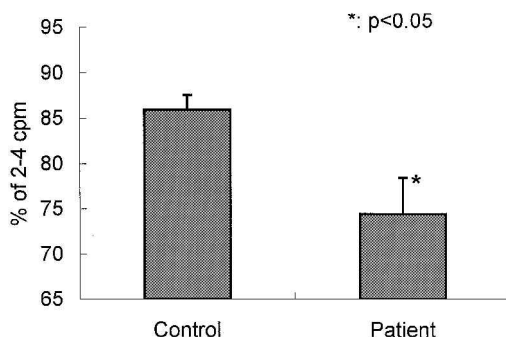


Fig 1. Percentage of normal 2–4 cpm waves in the fed state in patients with functional dyspepsia and healthy controls.

0.03); however, each itemized dysrhythmia was not significantly different between the two groups (patients vs controls): tachygastric ( $7.1 \pm 2.5\%$  vs  $4.6 \pm 1.4\%$ ,  $P > 0.05$ ); bradygastric ( $10.5 \pm 2.2\%$  vs  $5.4 \pm 1.4\%$ ,  $P > 0.05$ ); arrhythmic ( $8.0 \pm 2.1\%$  vs  $4.2 \pm 1.0\%$ ,  $P > 0.05$ ). The healthy controls had a mean percentage of 2–4 cpm waves of  $85.7 \pm 1.6\%$  in the fed state. In contrast, the patients had a mean percentage of 2–4 cpm waves of  $74.4 \pm 4.0\%$  ( $P < 0.03$ , in comparison with normal controls, see Figure 1). Figures 2 and 3 present EGG recordings and their running spectra in the fed state measured from a healthy subject and a patient, respectively. It can be seen that the EGG in the healthy subject had more regular 3 cpm slow waves than that in the patient. Using the definition of abnormal EGG rhythmicity described in the previous section, we found that patients with functional dyspepsia also showed a significantly higher prevalence of abnormal rhythmicity in the fed state in comparison with the controls. All healthy subjects had normal EGG rhythmicity ( $>75.5\%$ ), whereas six of 14 patients (42.9%) had an abnormal EGG rhythmicity ( $<75.5\%$ ) ( $P < 0.01$ ).

Different responses to the test meal in the power of the EGG at the dominant frequency (also called dominant power) were observed between the patients and the controls. The patients showed a smaller increase of dominant power after the test meal. As shown in Figure 4, the healthy subjects had an average increase of  $2.24 \pm 0.88$  dB ( $P < 0.03$  in comparison with fasting state) in the dominant power of the EGG (3 dB increase in power is equivalent to a 50% increase in the amplitude of the EGG), whereas the patients had an average decrease of  $-0.52 \pm 0.92$  dB ( $P < 0.05$  in comparison with the controls). Using the definition of abnormal postprandial EGG power (a decrease after meal), it was found that four of 13 controls (30.8%) had an abnormal response to the

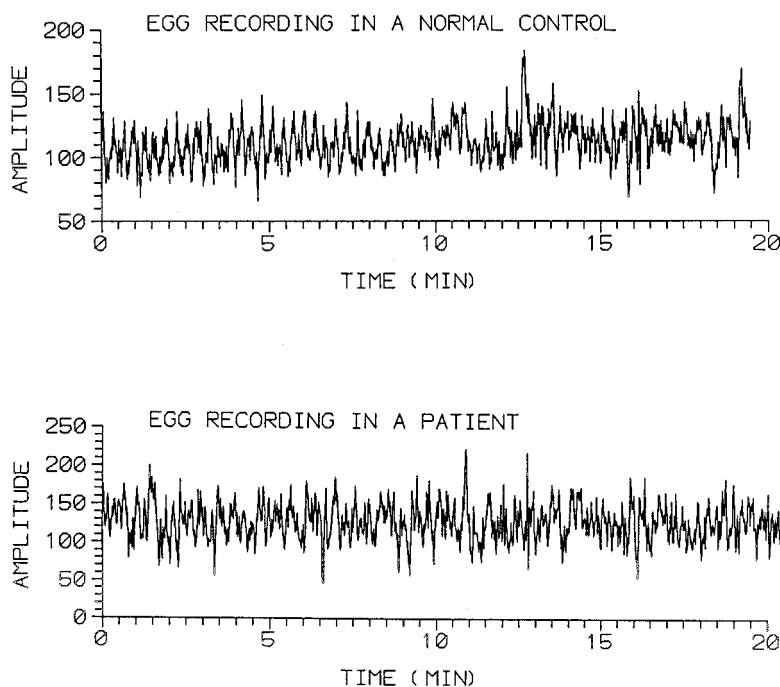


Fig 2. A portion of postprandial EGG in a healthy control (top) and a patient (bottom).

test meal, whereas nine of 14 patients (64.3%) had an abnormal response to the test meal. The prevalence of this abnormal response to the test meal was significantly higher in the patients than controls ( $P < 0.01$ ).

The patients showed a larger variation of the dominant frequency in both fasting and fed states. The dominant frequency in the controls ranged from 2.7 to 3.16 cpm in the fasting state and 2.57 to 3.63 cpm in the fed state ( $P < 0.01$  in comparison with fasting state), whereas that in the patients it varied from 0.86 to 3.28 cpm in the fasting state and 2.34 to 3.63 cpm in the fed state. However, there was no significant difference between the patients and the controls.

Patients also showed a higher value of the IC of the dominant frequency in both fasting and fed states (fasting:  $0.39 \pm 0.06$ , fed:  $0.33 \pm 0.04$ ), in comparison with controls (fasting:  $0.29 \pm 0.04$ , fed:  $0.27 \pm 0.02$ ). The difference was not statistically significant, however.

It was also found that some of the EGG parameters could be used to distinguish between the patients with functional dyspepsia and the healthy controls. As seen in Table 2, both the percentage of the 2–4 cpm and IC could be used to predict functional dyspepsia with 100% specificity or positive predictive value. The sensitivity or negative predictive value was low, however.

The average total symptom score was  $0 \pm 0$  for the healthy controls, and  $9.1 \pm 0.7$  for the patients with functional dyspepsia. No quantitative correlation was noted between any of the EGG parameters and the severity of the symptoms.

## DISCUSSION

In this study, we have found that the EGG in patients with functional dyspepsia had a significantly lower percentage of regular 2–4 cpm slow waves in the fed state and an abnormal response to the test meal in the dominant power of the EGG. It was also shown that some of the EGG parameters might be used to predict functional dyspepsia with a high specificity but a low sensitivity.

The EGG pattern in healthy controls has been reported in a number of previous studies (19, 31, 34–36). In these studies, the reported average value of the percentage of 2–4 cpm slow wave was between 75% to 90% in both fasting and fed states. The results in this study were consistent with these previous findings: the percentage of the 2–4 cpm waves was above 70% in both fasting and fed states, and there was a significant increase in dominant power as well as in dominant frequency after the test meal.

The major abnormalities observed in patients with

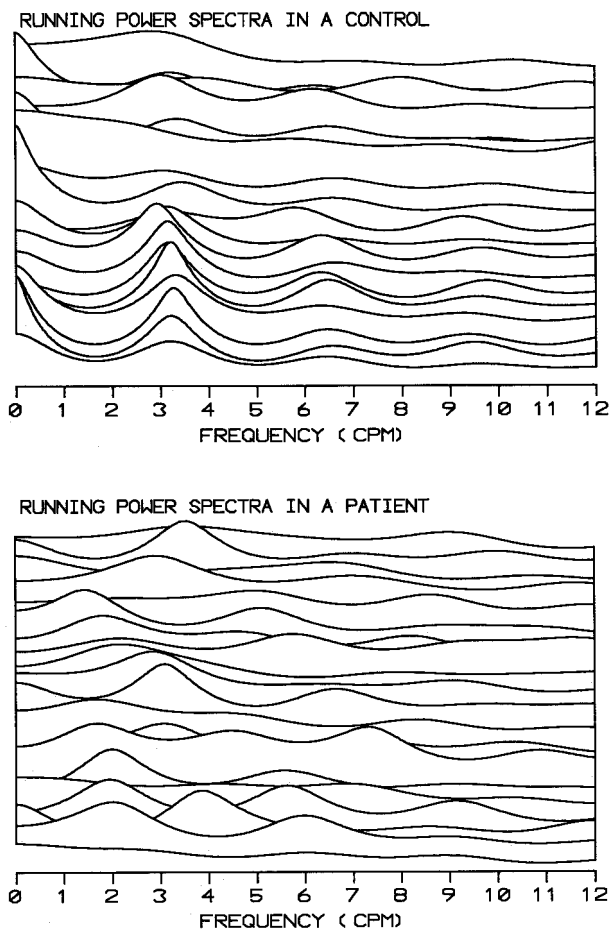


Fig 3. The running spectra of the EGG data presented in Figure 2. Lower panel is the running spectrum of the patient, top panel is the running spectrum from the control.

functional dyspepsia were the abnormality in the rhythmicity of the gastric slow wave in fed state and an absence of postprandial increase in the dominant power. These findings were similar to previous studies in patients with various gastric motor disorders. Sim-

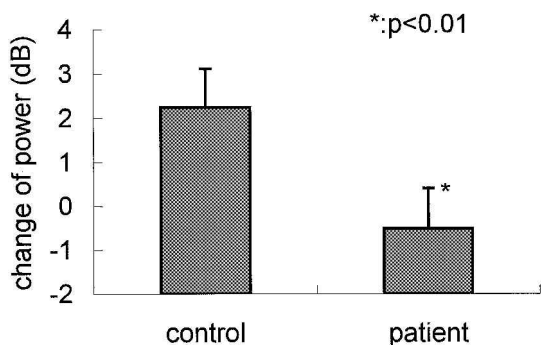


Fig 4. Change of EGG dominant power after the test meal in healthy controls and patients.

TABLE 2. PREDICTION OF FUNCTIONAL DYSPEPSIA USING EGG PARAMETERS\*

Parameter	Definition of abnormality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
2-4 cpm % (fed)	<75.5%	42.9	100	100	61.9
IC (fed)	>0.47	21.4	100	100	54.2

\* PPV: positive predictive value; NPV: negative predictive value.

ilar reduced slow wave rhythmicities and reduced postprandial increase in dominant power were frequently observed in patients with gastroparesis (9, 10, 22, 37, 38). Using 75.5% of the 2-4 cpm slow waves as the criterion for the definition of the abnormality of the EGG, we found that about 43% of the patients with functional dyspepsia had an abnormal postprandial EGG. This was comparable to the data reported in pediatric patients with functional dyspepsia. Riezzo et al previously investigated the effect of cisapride on gastric myoelectrical activity and gastric emptying in children with functional dyspepsia and reported similar abnormalities in the EGG (5).

The results of this study were comparable with those reported by Jebbink et al (18). Both studies reveal no significant difference in the dominant frequency of the EGG between the patients and controls, although the patients showed a larger variation in the fasting state. No specific dysrhythmias, such as tachygastria or bradygastria was found in either of the two studies. The total percentage of various dysrhythmias was noted to be significantly higher in the patients in this currently study; however, this was not available in the previous study. The average postprandial increase in power was observed to be lower in the patients in both studies. It was not significant in the previous study but was significant in the current study. This discrepancy might be attributed to the different test meals used: the test meal in the current study was bigger than in the previous one (475 vs 270 kcal). This suggests that a larger meal is more provocative in inducing abnormalities in patients. In a recent study, we compared the effects of meals with different calories on postprandial EGG (39). It was found that a small meal (170 kcal) was not able to induce the expected postprandial pattern of gastric myoelectrical activity.

This study has also shown that some of the EGG parameters may be used to distinguish between healthy controls and patients with functional dyspepsia. The specificity and the positive predictive value were high when postprandial rhythmicity was used as the predictor, whereas the sensitivity and negative predictive value were low. This implies that regular

gastric myoelectrical activity is a necessary but not sufficient condition for normal function of the stomach. This is in agreement with our previous findings in which the abnormal EGG was found to be able to predict delayed gastric emptying (37). The abnormalities observed in the EGG in that previous study suggested that irregular gastric slow waves may result in gastric hypomotility and/or uncoordinated gastric contractions, leading to a delayed emptying of the stomach. The association between abnormal gastric myoelectrical activity and gastrointestinal symptoms, such as nausea and vomiting, has been reported previously (8–10), but no significant correlations were found in this study.

In this study we also computed the instability coefficient of the dominant frequency and found that this parameter is useful in the assessment of patients with functional dyspepsia. No previous studies have systematically investigated this parameter, and thus no comparison could be made.

In summary, functional dyspepsia patients as a group demonstrate abnormal postprandial gastric myoelectrical activity, including reduced normal 2–4 cpm waves and abnormal response in its amplitude to the test meal.

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