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Inhibitory effects of stress on postprandial gastric myoelectrical activity and vagal tone in healthy subjects

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Abstract *The aim was to investigate gastric myoelectrical activity (GMA) and vagal activity in response to stress. The study was performed in 10 healthy subjects in three sessions (control, relaxation and stress). The control session was composed of 30-min recordings before and 30-min recordings after a test meal. The protocol of two other sessions was similar except that the fasting recording was extended to 60 min and the subjects were continuously watching a horror movie (stress) or guided meditation tape (relaxation) after the 30-min baseline. GMA was recorded using electrogastrography and heart rate variability (HRV) was derived from the electrocardiogram. Meal resulted in a postprandial increase in the dominant frequency (2.91 cpm vs 3.17 cpm, $P < 0.007$), dominant power (30.0 dB vs 32.5 dB, $P < 0.05$), and percentage of normal slow waves (79.8% vs 87.4%, $P = 0.09$). Similar responses were found in the relaxation session. Stress inhibited all these normal postprandial response and reduced the regularity of gastric slow waves (82.0% vs 66.0%, $P < 0.01$). In addition, spectral analysis of the HRV demonstrated an inhibition of postprandial vagal activity and an increase of postprandial sympathetic activity with stress. Stress has an inhibitory effect on postprandial GMA and this may involve both vagal and sympathetic pathway.*

Keywords *electrogastrography, gastric motility, gastric myoelectrical activity, heart rate variability, stress.*

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INTRODUCTION

Stress is defined as acute threats to the homeostasis of an organism, either physically or psychologically, and has long been documented to alter gastrointestinal motility through a brain-gut network.[1,2] A number of studies have demonstrated that stress impairs gastroduodenal motility,[3–5] delays gastric emptying,[6,7] and alters intestinal transit[8,9] and colonic motility.[10] Due to its prominent role in physiological and pathophysiological processes of gastrointestinal motility, stress has also been used as a means of studying brain-gut interactions.

Gastric myoelectrical activity (GMA) plays an important role in the regulation of gastric motility.[11] GMA is composed of slow waves and spikes. The gastric slow wave is an omni-present rhythmic electrical event with a frequency of three cycles per min (cpm) in humans. It determines the frequency and propagation of gastric contractions. Spikes, when present, are superimposed on slow waves and indicative of gastric contractions. Non-invasive electrogastrography is a common method for the measurement of GMA.[12] It has been shown that the electrogastrogram (EGG) is an accurate measure of gastric slow waves and its relative amplitude change reflects gastric contractility.[13–15]

Little is known on the effects of stress on GMA or slow waves. Stern *et al.* reported that, in healthy volunteers, cold stress attenuated the amplitude of normal 3 cpm gastric slow wave in the fed state but not in the fasting state.[16,17] Considered as a form of stress, motion sickness has been consistently shown to decrease normal 3 cpm activity and increase 4–9 cpm tachygastria.[18–20] Muth *et al.* used a psychological stress (a threat of shock if reaction was too slow) and invoked gastric dysrhythmia (tachyarrhythmia).[17] Electrogastrography was used in these studies. As the gastric slow wave is of a very low frequency (only three waves in a minute), a prolonged recording of the EGG

is usually required in order to derive an accurate spectral analysis.[21] However, stress used in the previous studies was of a brief duration. To solve this problem, a unique stressor was selected in this study: individualized horror movies. It induced emotional stress with a prolonged duration and is suitable for electrogastrography (does not induce motion artefacts).

It has been reported that stress alters vagal activity, and changes in gastrointestinal motility may be attributed to the alteration in vagal activity.[22,23] However, little is available in the literature regarding the possible association between alterations in vagal activity and alterations in GMA. Spectral analysis of heart rate variability (HRV) provides a non-invasive assessment of vagal activity, and is not only frequently used in cardiac research but also applied in gastrointestinal research.[24–26]

The aims of this study were to investigate GMA in response to a horror movie using non-invasive electrogastrography, and to evaluate the involvement of vagal activity with stress using the spectral analysis of HRV.

MATERIALS AND METHODS

Subjects

Ten healthy volunteers were recruited in this study, including four males and six females, aged 43.2 ± 2.2 years. None of the subjects had any gastrointestinal diseases or symptoms or a history of gastrointestinal surgery. All women were studied during their follicular phase of the menses to minimize possible hormonal influences.[27] No medications were used by the participants except oral contraceptives. The study was approved by the Institutional Review Board at Integris Baptist Medical Center in Oklahoma City. Written consent was signed by the subjects before the study.

Experimental protocol

The experiment consisted of three sessions (control, relaxation and stress) on three separate days in a randomized order. The control session was composed of a 30-min baseline recording in the fasting state (after a fast of 6 h or more) and 30-min after a standard test meal. The protocol of the other two sessions was the same except that the fasting recording was extended to 60-min and the subjects was continuously watching a horror movie (stress session) or a guided meditation tape (relaxation session) during the 30-min immediately before and 30-min immediately after the meal. The horror movie was chosen individually based on an interview performed before the study. The EGG and electrocardiogram (ECG) were recorded simultaneously during the entire session. The subject was in a supine position and was instructed to minimize their movements during the entire recording period. Talking or reading was not allowed. The test meal was composed of 475 kcal, with 21% of protein, 17% of fat and 62% of carbohydrate.

Electrogastrogram

Surface EGG was applied to record GMA. Before the attachment of electrodes, the abdominal skin of recording sites was cleaned with sandy skin-prep jelly (OMNI PREP, Weaver & Co., Aurora, CO, USA) to reduce the impedance. The skin was rubbed until pinkish, and the hair, if present, was shaved. Three silver/silver chloride ECG electrodes (SNAP, Lombard, IL, USA) were placed on the abdominal skin. One electrode was placed at the midpoint between the xiphoid and the umbilicus; the other one was placed on the 45-degree line, 5 cm above and to the left of the first one. The last electrode was placed at the left flank beneath the rib cage. Two epigastric electrodes were connected to yield a bipolar EGG signal, while the last electrode was used as a reference. The EGG signal was amplified using a portable EGG recorder (Digitrapper EGG, Synectics Medical, Inc., Irving, TX, USA) with a low cut-off frequency of 1 cpm and a high cut-off frequency of 18 cpm. On-line digitization with a sampling frequency of 1 Hz was performed using an analogue/digital converter installed on the recorder, and digitized samples were stored on the recorder.

Analysis of gastric myoelectrical activity

At the end of the study, the data saved in the EGG recorder were uploaded to an IBM 486 personal computer. Data obtained during the 30-min baseline recording and the 30-min postprandial period in each session were subjected to computerized spectral analysis using programs previously developed in our laboratory.[28] (Fig. 1) The pattern of the EGG was characterized by several quantitative parameters, including the dominant frequency, dominant power and percentage of normal 2–4 cpm slow waves, as well as the instability coefficient of dominant frequency, which are described below.

Dominant frequency and power of the EGG The frequency at which the EGG power spectrum has 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 the implanted serosal electrodes.[13–15] Smoothed power spectral analysis was used to produce an averaged power spectrum of the EGG for each recording period. The power at the dominant frequency in the power spectrum of the EGG was defined as the EGG dominant power. It was shown that the relative change of the EGG dominant power reflects gastric contractility.[15,29]

Percentage of regular 2–4 cpm slow waves The percentage of normal 2–4 cpm gastric slow waves, which reflects the regularity of gastric slow waves, was defined as the percentage of time during which normal 2–4 cpm slow waves were present over each 30-min recording period. It was computed from the running power spectra of the EGG using an adaptive spectral analysis method.[30] 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 whether the peak power was within the range of 2–4 cpm. The 1-min recording was defined as normal if it had a clear peak in the 2–4 cpm range. Otherwise, it was defined as dysrhythmic.

Instability coefficient of the dominant frequency Instability coefficiency of the dominant frequency was referred as the minute-by-minute variation of the dominant frequency of the EGG. It was defined as the ratio between the standard deviation of the dominant frequencies and the mean dominant frequency over the 30-min period.[21]

Electrocardiogram

The ECG was recorded using a special one-channel amplifier with a cut-off frequency of 100 Hz (Model 2283 Fti Universal Fetrode Amplifier, UFI, Morro Bay, CA, USA) from two separate leads and one ground electrode. The two leads were attached to the left and right superclavicular fossas of the subjects and the ground to the left leg. The data were digitized online at 1000 Hz using a 486 IBM-compatible PC and a data acquisition package (Alice 3, Healthdyne Technologies, Inc., Marietta, GA, USA). The HRV signal was derived from the ECG recording using a special program developed in our laboratory[31] by identifying R peaks, calculating R-R intervals, interpolating the R-R intervals so that the time interval between consecutive samples was equal and finally down-sampling the interpolated data to a frequency of 1 Hz.

Analysis of heart rate variability

Overall power spectral analysis was applied to the HRV signal and the power in each frequency sub-band was calculated. The power in the low frequency band (0.04–0.15 Hz), LF, represents mainly sympathetic activity and part of parasympathetic activity. The power in the high frequency band (0.15–0.50 Hz), HF, stands purely for parasympathetic or vagal activity. LF was defined as the area under the curve in the frequency range of 0.04–0.15 Hz and HF was defined as the area under the curve in the frequency range of 0.15–0.50 Hz. The LF/HF ratio reflects the balance between sympathetic activity and vagal activity.

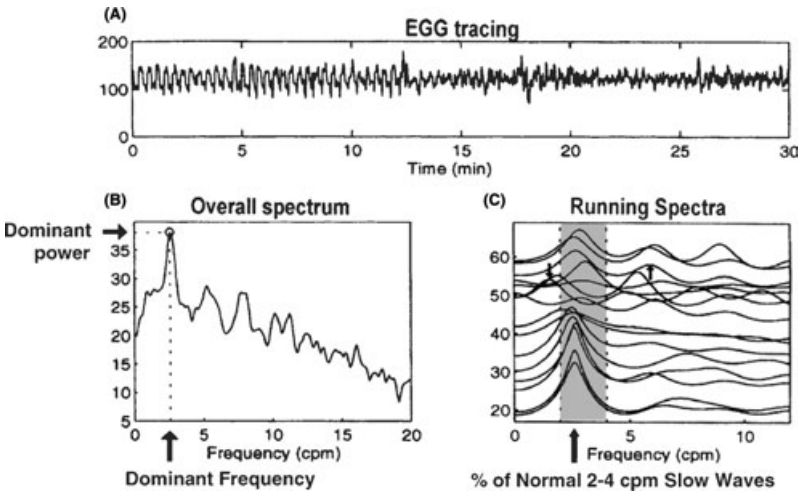

Figure 1 Recording and analysis of gastric myoelectrical activity. (A) A tracing of EGG. (B) Power spectrum: the peak values were defined as the dominant frequency and dominant power. (C) Running spectrum: the segment of data was defined as normal if its dominant peak was in the frequency range of 2–4 cpm.

Statistical analysis

All data were presented as means ± SE. Paired student's *t*-test was applied to investigate the difference in each of the EGG parameters between the baseline (fasting) and postprandial data. ANOVA was used to compare postprandial changes in vagal activity among the three sessions. A *P*-value of <0.05 was considered statistically significant.

RESULTS

Gastric myoelectrical activity

All data regarding the EGG are presented in Table 1. Regular gastric slow waves were recorded at baseline in each session and no difference was noted among the three sessions. However, different postprandial responses of GMA were noted in the three sessions described as follows.

Normal postprandial responses to the test meal, comparable to the data published in the literature, were observed in the control session. The dominant frequency of EGG at baseline was 2.91 ± 0.04 cpm and significantly increased ($P < 0.007$) to 3.17 ± 0.09 cpm after the meal (Fig. 2). The power at the dominant frequency was also increased ($P < 0.05$) from 30.0 ± 2.8 dB at baseline to 32.5 ± 2.6 dB after the meal (Fig. 3). The instability coefficient of the dominant frequency showed no significant postprandial change (0.28 ± 0.05 *vs* 0.27 ± 0.02, $P > 0.05$) (Fig. 4). The percentage of 2–4 cpm slow waves showed a noticeable increase, which was, however, not statistically significant (79.8 ± 5.0% *vs* 87.4 ± 3.5%, $P = 0.09$) (Fig. 5).

Similar normal postprandial responses to the test meal were noted in the relaxation session. The dominant frequency of EGG at baseline was 2.83 ± 0.09 cpm and significantly increased ($P < 0.03$) to 3.09 ± 0.07 cpm after the meal (Fig. 2). The dominant power was increased ($P < 0.02$) from 26.4 ± 2.9 dB at baseline to 31.3 ± 1.8 dB after the meal (Fig. 3). The instability coefficient of dominant frequency was decreased from 0.36 ± 0.04 to 0.21 ± 0.04 ($P < 0.02$) suggesting more stable slow wave frequencies (Fig. 4). The percentage of normal 2–4 cpm slow waves was 76.0 ± 7.0% at baseline and increased to 82.0 ± 6.0% after the meal although statistically not significant ($P = 0.10$) (Fig. 5).

Stress completely inhibited the normal postprandial responses of GMA. In the stress session, the dominant frequency was 2.92 ± 0.06 cpm at baseline and did not change after the meal (2.83 ± 0.11 cpm, $P > 0.05$) (Fig. 2). The dominant power did not show a postprandial increase (22.6 ± 2.1 dB *vs* 24.9 ± 2.4 dB, $P > 0.05$) (Fig. 3). Instead of a decrease as observed in the relaxation session, the postprandial instability coefficient of dominant frequency showed an increase, although not statistically significant, in comparison with the fasting state (0.44 ± 0.04 *vs* 0.35 ± 0.07, $P = 0.9$). It was, however, significantly higher ($P < 0.001$) than the corresponding value in the relaxation session. Moreover, the percentage of normal 2–4 cpm slow waves was significantly decreased ($P < 0.01$) from 82.0 ± 5.0% at baseline to 66.0 ± 5.0% after the meal under stress (Fig. 5).

Vagal activity

Vagal activity assessed by the spectral analysis of the HRV was significantly different among control, relaxation and stress sessions (ANOVA, $P < 0.05$). Postprandial vagal activity (HF) was decreased in all sessions (21.90 ± 2.10 *vs* 17.00 ± 1.80 in the control session; 19.61 ± 1.52 *vs* 16.36 ± 1.61 in the relaxation session; 19.09 ± 2.10 *vs* 9.59 ± 1.70 in the stress session; all baseline *vs* postprandial, $P < 0.05$). However, the postprandial decrease was significantly higher in the stress session (9.50 ± 3.07) than that in the control (4.90 ± 1.70) and relaxation (3.25 ± 1.21) sessions ($P < 0.04$). Postprandial sympatho-vagal balance (LF/HF) was increased in all sessions (1.78 ± 0.33 *vs*

Table 1 Gastric myoelectrical activity in three sessions: control, relaxation and stress

	Control		Relaxation		Stress	
	Preprandial	Postprandial	Preprandial	Postprandial	Preprandial	Postprandial
DF (cpm)	2.91 ± 0.04	3.17 ± 0.09*	2.83 ± 0.09	3.09 ± 0.07*	2.92 ± 0.06	2.83 ± 0.11
DP (dB)	30.0 ± 2.8	32.5 ± 2.6*	26.4 ± 2.9	31.3 ± 1.8*	22.6 ± 2.1	24.9 ± 2.4
Icdf	0.28 ± 0.05	0.27 ± 0.02	0.36 ± 0.04	0.21 ± 0.04*	0.44 ± 0.04	0.35 ± 0.07
N%	79.8 ± 5.0	87.4 ± 3.5	76.0 ± 7.0	82.0 ± 6.0	82.0 ± 5.0	66.0 ± 5.0*

*$P < 0.05$ *vs* Preprandial.
DF, Dominant frequency of the ECG; DP, Dominant power of the ECG; N, Normal percentage of the ECG.

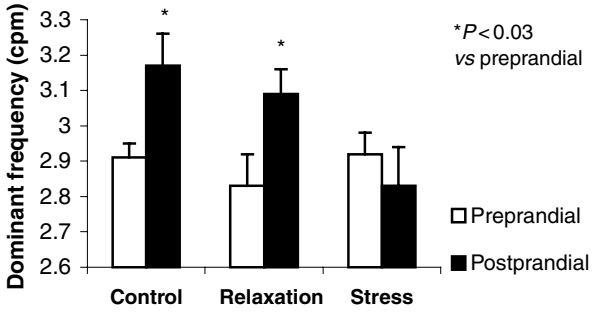

Figure 2 Effects of stress on dominant frequency of EGG. In the control and relaxation sessions, the dominant frequency of the EGG was significantly increased ($P < 0.03$) after the meal. In the stress session, the dominant frequency was not changed after the meal.

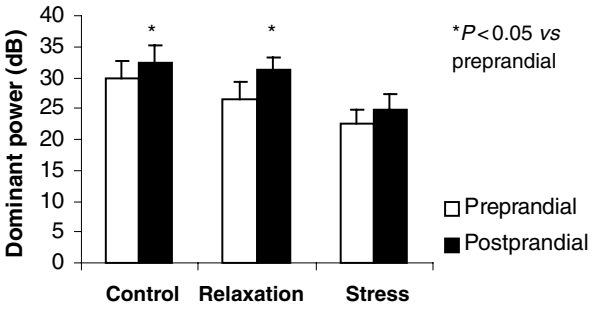

Figure 3 Effects of stress on dominant power of EGG. In the control and relaxation sessions, the dominant power was markedly increased ($P < 0.05$) after the meal compared with that before the meal. In the stress session, the dominant power did not differ after the meal.

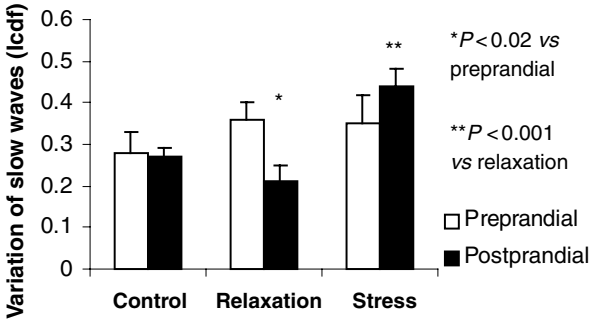

Figure 4 Effects of stress on slow wave variation. In the relaxation session, the instability coefficient of dominant frequency was significantly decreased ($P < 0.02$). Slight decrease was observed in the control session, but statistically, not significant. In the stress session, although postprandial instability coefficient of dominant frequency was not different from that before the meal, it was much bigger than that postprandial number ($P < 0.001$) in the relaxation session.

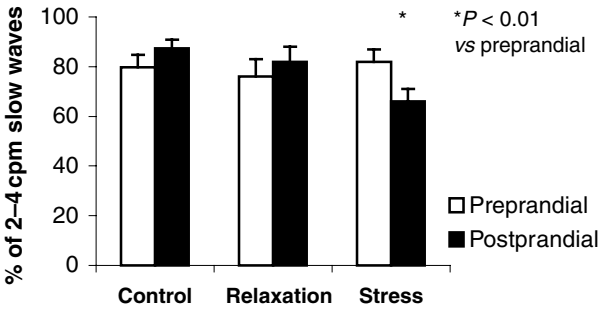

Figure 5 Effects of stress on regularity of slow waves. In the control and relaxation sessions, the percentage of normal 2–4 cpm slow waves was seemed to be increased, but not statistically significant ($P > 0.05$). In the stress session, the percentage of normal 2–4 cpm slow waves was significantly decreased in the fed state ($P < 0.01$).

2.57 ± 0.40 in the control session; 1.80 ± 0.30 *vs* 2.52 ± 0.32 in the control session and 1.89 ± 0.67 *vs* 3.20 ± 0.50 in the stress session; all baseline *vs* postprandial, $P < 0.05$). Similar to the vagal activity, a significantly higher postprandial increase was noted with stress in the LF/HF (1.31 ± 0.80 in the stress session, 0.79 ± 0.40 in the control session and 0.72 ± 0.40 in the relaxation session, $P < 0.02$, see Fig. 6). The postprandial LF was significantly increased from 28.50 ± 2.70 to 40.90 ± 1.90 ($P < 0.05$) compared with the baseline in the stress session. Whereas, no significant difference was observed in the postprandial LF in either control or relaxation session (28.20 ± 2.6 *vs* 32.10 ± 4.50 in the control session, 29.00 ± 2.50 *vs* 31.30 ± 2.70 in the relaxation session; baseline *vs* postprandial, $P > 0.05$).

DISCUSSION

The data in this study have shown that a standard test meal resulted in a postprandial increase in the dominant frequency, dominant power, and percentage of normal 2–4 cpm gastric slow waves. The relaxation with the guided meditation tape did not alter these postprandial responses. The stress, however, inhibited all these normal postprandial responses and reduced the regularity of gastric slow waves. A similar postprandial inhibitory effect on vagal activity was concurrently noted with the stress.

In this study, we investigated the brain-gut connection by assessing gastric function in response to psychological stress. Gastric function was assessed by the measurement of GMA. Due to the nature of the gastric pacemaker activity, a unique stressor was chosen to produce a prolonged stimulation. The simultaneous recording of HRV allowed us to examine

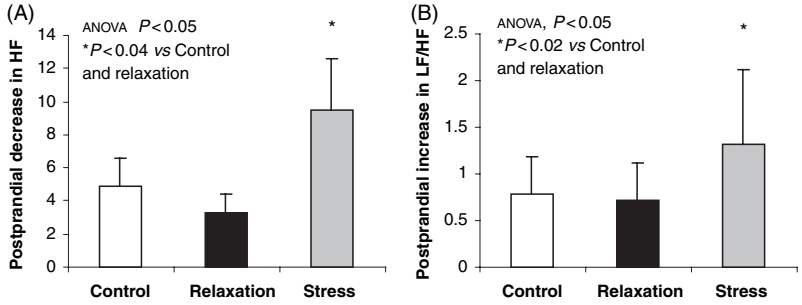

Figure 6 Effects of stress on postprandial vagal activity. There was a significant difference among the control, relaxation and stress sessions both in A and B (ANOVA, $P < 0.05$). (A) Stress resulted in a higher postprandial decrease in vagal activity compared with control, relaxation ($P < 0.04$). (B) Stress resulted in a higher postprandial increase in sympatho-vagal balance compared with control, relaxation ($P < 0.02$).

vagal activity, which mediates the interaction of the brain and the enteric nervous system. In addition, we added a session of meditation to counter-act the stress effect on the gastric and vagal/autonomic functions.

Stress has been shown to have an inhibitory effect on gastric motility and may play a role in the aetiology in functional gastrointestinal disorders such as functional dyspepsia. Camilleri et al measured postprandial antral motility using gastrointestinal manometry and found that antral motility was decreased under stress induced by a transcutaneous electrical nerve stimulator in healthy volunteers, but was normal or suppressed in functional dyspepsia patients.[3] This inhibitory effect of stress on antral motility was confirmed in a study by Fone *et al.*[6] Mearin *et al.* reported that cold stress induced a gastric relaxatory response measured by gastric barostat in dyspeptics.[5] Thompson *et al.* revealed a significant delay in gastric emptying of a liquid meal with cold stress.[4]

Among a few studies investigating the effect of stress on gastric slow waves, there was a large variation in methodologies, mainly in the choice of stressors. A reliable and accurate analysis of the EGG, as well as HRV, requires a prolonged and motion artifact-free recording. Accordingly, a stressor that lasts briefly or a stressor that involve any kind of motion or physical activities would be inadequate for the EGG study. These limitations led us to look for a stressor that is of a long duration and requires only passive participation of the subject. We found that TV watching fulfilled both of these requirements. An individually chosen horror movie was applied as the stressor, while a meditation tape served as a comparison. We would like to point out the fact that all participants stated at the end of the study that the videotapes were effective in inducing the psychological effect desired for the relevant sessions.

Our study demonstrated a marked inhibitory effect of stress on postprandial GMA. GMA is known to have a regulatory effect on gastric motility. Numerous studies have reported the association between GMA and gastric motility.[32–34] Enhanced GMA is associated with increased gastric motility, whereas impaired GMA, i.e. gastric dysrhythmia, has been frequently reported in patients with gastric motility disorders.[35,36] The postprandial responses of GMA measured from the EGG in either the control or the relaxation session was in agreement with those published previously. Firstly, there was a slight but significantly increase in the frequency of the gastric slow wave. This postprandial increase was frequently noted after a solid meal but not a liquid meal (a pure liquid meal may result in a decrease in slow wave frequency).[37] In this study, a solid test meal was used. Secondly, there was a significant increase in the dominant power of the EGG. Although the EGG is not a direct measurement of gastric contractions, numerous studies have shown that a relative increase in the amplitude (or power at 3 cpm slow wave frequency) of the EGG reflects increased gastric contractility.[15,33] Thirdly, the percentage of normal slow waves was increased although not statistically significant. Under the normal condition, the postprandial EGG showed a trend of increase in the percentage of normal slow waves.[38] However, the increase would not reach the statistical significance in healthy volunteers attributed to the fact that the slow wave is already normal in the fasting state. However, a significant smaller variation in slow wave frequency is often noted in the postprandial state in the healthy volunteers,[39,40] reflected as a decrease in the instability coefficient of the dominant frequency of the EGG, as seen in the relaxation session of this study. The stress used in this study abolished all these normal postprandial responses, demonstrating an

inhibitory effect of the stress on postprandial GMA. A similar inhibitory effect of stress on postprandial gastric slow waves was reported in a previous study by Stern *et al.*[16] They used cold stress and found a reduction in 3 cpm slow wave activity in the fed state without clear evidence of dysrhythmia.

Motor activity of the stomach, like other regions of the gut, is regulated by changes in the vagal activity. The effects of stress on myoelectrical activity may be secondary to changes in vagal tone. We, therefore, measured vagal activity by using spectral analysis of the HRV and its responses to stress. Spectral analysis of HRV is an established non-invasive method for the quantitative evaluation of autonomic activity.[31,41,42] The complete information derived from the spectral analysis of HRV included LF, HF and LF/HF. We presented data on HF, and LF/HF as well as LF. Previous studies with autonomic blocking drugs, postural changes, and cross-spectral analyses suggested that LF does not reflect pure sympathetic activity, but primarily sympathetic activity with some parasympathetic components.[43–45] HF is known to represent pure parasympathetic (vagal) activity and LF/HF is a reliable indicator of sympatho-vagal balance. In the current study, a significant postprandial decrease in vagal activity and a significant increase in sympathovagal balance were noted with the stress. This finding suggests that the vagus may mediate some of the visceral effect of stress. Although the LF is not a pure indicator of sympathetic activity, the significant and substantial increase in the value of LF suggests that the sympathetic pathway is also involved with the stress in this study. Most of the published data on stress have indicated that the adrenergic effects outweigh the cholinergic ones. Autonomic dysfunction has been frequently reported in patients with gastrointestinal motility disorders.[24,41] Muth *et al.*[17] reported that stress increased sympathetic activity in health volunteers with an associated gastric dysrhythmia. Although an accurate assessment of sympathetic activity cannot be obtained from the spectral analysis of the HRV, the increased sympthovagal balance and the decrease in vagal activity with stress observed in this study were indicative of an increase in sympathetic activity.

In conclusion, stress has inhibitory effects on postprandial GMA, and these inhibitory effects may involve both vagal and sympathetic pathway.

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