Transfer Function Analysis of Heart Rate Variability Correlated with Gastric Myoelectrical Activity Using a Liquid Nutritional Meal Compared to Water: Are They Different?

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Abstract

We aimed to investigate difference in the effects of water and a liquid nutritional meal on the parasympathetic and gastric myoelectrical activities. The study was a repeated-measures design in which each subject was presented with 500 ml of water and a liquid nutritional meal (Ensure®) on two separate and random sessions. The electrogastrography (EGG) and electrocardiogram were simultaneously recorded in 16 healthy subjects. There were no significant changes in the EGG-3 cycle per minute (cpm) power, any HRV variable, or the transfer function magnitude after Ensure® intake. Water ingestion resulted in a significant increase in both the EGG-3 cpm power and the transfer magnitude compared to Ensure® intake ($P < 0.05$). The effects of water and Ensure® on the parasympathetic and gastric electric activities are different, in which the latter is less likely to provoke an autonomic response after gastric stimulation.

Key Words: autonomic nervous system, gastric myoelectrical activity, heart rate, respiration

Introduction

Electrogastrography (EGG) has been a widely used technique to record gastric myoelectrical activity. It is a noninvasive method used to obtain a cutaneous recording of gastric electrical and mechanical activity from the upper abdominal surface (7, 8). The mechanical activity of stomach is controlled by gastric myoelectrical activity which originates at a pacemaker site in the proximal body and propagates to the distal antrum at a frequency of about 0.05 Hz (3 cpm) (15). Using spectral analysis of EGG, previous studies have shown its relationship with gastric motor activity (1, 30). It is generally accepted that a wave around 0.05 Hz represents normal gastric slow wave (1, 30, 32). Many studies have shown a postwater or postprandial power increase (9, 12, 17). The relative change of EGG power from before to after certain stimulation is thought to be of clinical significance (8, 12) and may correspond to vagal nerve activity. Different responses of gastric myoelectrical activity to liquid and solid meals have been reported (5, 6).

Frequency-domain analysis of heart rate variability (HRV) is a noninvasive tool for the evaluation of autonomic regulation of the heart. HRV can be categorized into high-frequency (HF; 0.15-0.40 Hz)

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and low-frequency (LF; 0.04-0.15 Hz) components according to its oscillating frequency and developing mechanism (33). The HF component is equivalent to the well-known respiratory sinus arrhythmia (RSA) and is generally assumed to represent parasympathetic control of heart rate (11). The LF component is jointly contributed by both sympathetic and parasympathetic nerves (3). The ratio LF/HF is considered to mirror sympathovagal balance (2, 25) or to reflect sympathetic modulation (24-26). In a previous study, Saul *et al*. demonstrated that transfer function analysis of HRV and respiration can be efficiently determined over a range of physiologically important frequencies through the use of a broad-band respiratory input (29). It provides a precise and efficient characterization of RSA which can yield considerable insight into autonomic regulation of the heart. By using a similar method, we have previously demonstrated a significant increase in the EGG power as well as the respiration-HRV transfer magnitude after water intake (4). It has been concluded that transfer function analysis of HRV could be valuable to identify subtle changes in the RSA after water intake (4). The aim of this study was to utilize transfer function analysis of HRV and respiration to investigate any difference in the effects of water and a liquid nutritional meal (Ensure®) on gastric myoelectrical activity and cardiac parasympathetic activity. We hypothesized that Ensure® intake will provoke different autonomic responses compared with water ingestion.

Materials and Methods

Subjects

The study was performed in 16 healthy non-smoking subjects (women/men = 9/7, ages 21.5 ± 0.5 year) without symptoms or history of gastrointestinal, cardiovascular or other diseases. Their body mass index was 20.2 ± 0.6 (ranged from 17 to 28) kg/m^2. None had any medication for at least 2 weeks before or during the study. Subjects fasted for more than 6 h (most fasted overnight). Studies were accomplished with subjects' written informed consent, in accordance with the Helsinki Declaration.

Experiment Design

Each subject was presented with water and Ensure® on two separate sessions. All measurements were performed in the daytime (8:00-16:00), while each subject lay quietly and breathed normally in a quiet and air-conditioned (25°C) environment. The EGG and ECG data were recorded simultaneously and continuously as follows. First, the fasting data were collected for 10 min in the supine position. Then, the subjects were asked to sit up, drink 500 ml of distilled water (room temperature), and then again assume a supine position. The recording was stopped 30 min after the water intake. On a separate day, the same procedure was completed with a test meal (Ensure Liquid, Abbott, Taipei, Taiwan) which was served at room temperature and consumed without complaint regarding the taste of the test meal. The composition of the test meal was: 500 ml, 532 Kcal, 16.8 g protein, 13.0 g fat, and 86 g carbohydrate.

Recordings EGG and instantaneous chest circumference signals were recorded noninvasively by an integrated EGG machine (3 CPM company, Crystal Bay, NV, USA). Instantaneous chest circumference signals were used to quantify respiratory movements. All EGG, chest circumstance and ECG signals were simultaneously digitized using a 12-bit analog-to-digital converter (Advantech PCL1815, Taipei, Taiwan) at a sampling rate of 512 Hz. The digitized ECG signals were stored on a hard disk for off-line analysis.

Processing of ECG and Respiration Signals

Computer analysis of HRV and respiration-HRV transfer function have been detailed in our previous investigations (4, 19). In brief, the stationary R-R intervals (RR) were resampled and interpolated at the rate of 16 Hz. The sampling rate of respiration signals was also reduced to 16 Hz by averaging. The respiration and RR signals to be analyzed were truncated into 64-s (1,024 points) time segments with 50% overlap. For each time segment, the linear trend was removed and a Hamming window was applied (20). Power spectral analysis was accomplished by fast Fourier transform, and average periodograms were generated by averaging the autospectra from 8 time segments. Cross-spectral analysis was carried out on the same 8 sets of data on respiration and RR signals, which led to the computation of the two functions. First, a squared coherence function

$$k^2(f) = |S_{RH}(f)|^2 / [S_{RR}(f) \cdot S_{HH}(f)] \quad \text{(I)}$$

where $S_{RR}(f)$ and $S_{HH}(f)$ are the respective power spectra for respiration and RR signals, and $S_{RH}(f)$ is their cross spectrum. The k^2 ranges from 0 to 1, which provides an assessment of the linear relationship at each frequency of the statistical reliability of transfer function. A value ≥ 0.5 was taken to be statistically significant (10, 18). Second, a transfer function

$$H(f) = S_{RH}(f)/S_{RR}(f) \quad \text{(II)}$$

with a magnitude defined as

$$\{[H_R(f)]^2 + [H_I(f)]^2\}^{1/2} \quad \text{(III)}$$

where $H_R(f)$ and $H_I(f)$ are the real and imaginary parts of the complex $H(f)$ values and are expressed as ms per cm.

Processing of EGG Signals

The sampling rate of EGG signals was reduced to 8 Hz by averaging. The EGG signals to be analyzed were truncated into 128-s (1,024 points) time segments with 75% overlap. For each time segment, the linear trend was removed and a Hamming window in the time domain was applied. Power spectral analysis was accomplished by fast Fourier transform, and average periodograms were generated by averaging the autospectra from 6 time segments.

Statistical Analysis

Low-frequency (0.04-0.15 Hz) power (LF) and high-frequency (0.15-0.4 Hz) power (HF) of HRV was quantified by integration of its average periodogram in the specified ranges. The respiration-HRV transfer magnitude of the oscillating frequency and the power of EGG between 0.042-0.058 Hz (2.5-3.5 cycles/min) were quantified (4, 18). Oscillating frequency was selected. For comparing the effect of water and liquid meal on EGG and HRV parameters, we further determined the difference of a certain parameter X after water or liquid meal to that before water or liquid meal as ΔX (e.g., ΔHF = post-HF - pre-HF). All of the measured values are expressed as means ± SEM. Student's *t*-test was used as appropriate to determine significant differences. The statistical significance was defined as $P < 0.05$.

Results

Changes in Indices of HRV, EGG, and Resipration-HRV Transfer Function with Ensure®. The results of spectral analysis in these parameters are presented in Fig. 1. The autospectrum for respiration showed a power density in the frequency range of 0.2-0.4 Hz. Frequency-domain analysis of R-R intervals provided a more detailed observation of HRV. The dominant HF and recessive LF were clearly detected at 0.15-0.4 Hz and 0.04-0.15 Hz, respectively. The coherence function further demonstrated good linearity between respiration and HRV signals at ventilatory rate between 0.2 and 0.4 Hz before and after Ensure® intake. The average transfer magnitude was present in the frequency range of 0.2-0.4 Hz. The autospectrum for EGG signals revealed most power density over 0-0.2 Hz throughout Ensure® intake.

Fig. 2 shows the quantitative analysis of HRV, EGG, and respiration-HRV transfer function. There were no significant changes in the magnitude of the respiration-HRV transfer function and the EGG-3 cpm power throughout the study. There were also no significant changes in any HRV parameters during the test periods.

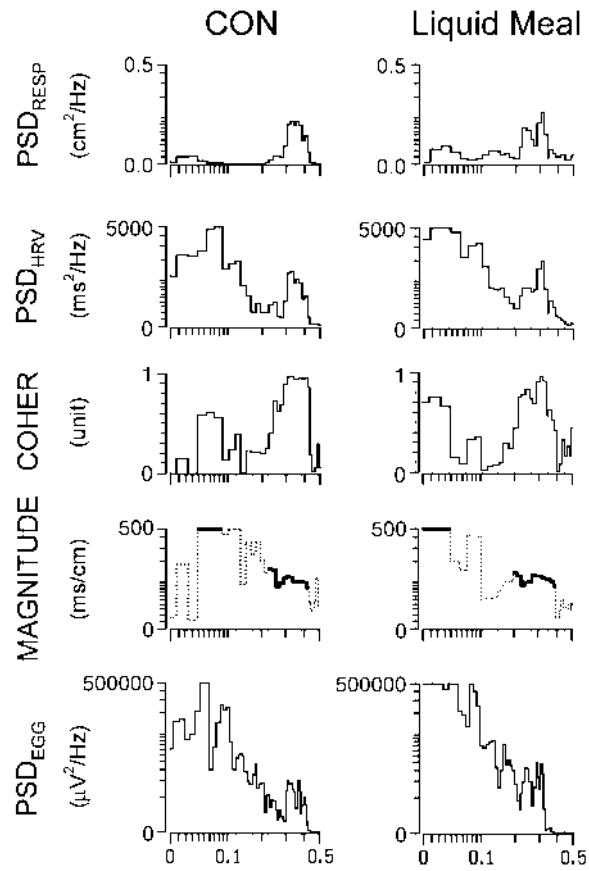

Fig. 1. The average periodograms of respiration (PSD_{RESP}) and heart rate variability (PSD_{HRV}) and cross-spectrograms showing coherence (COHER) and magnitude of transfer function (MAGNITUDE) generated before and after liquid meal (Ensure®) intake from a study subject. A coherence function ≥ 0.5 is considered to be statistically significant, and corresponding range of frequencies in magnitude of transfer function is denoted by a thick line. Also shown is the power spectral density of electrogastrogram (PSD_{EGG}).

Difference Between the Effect of Water and Ensure®. As can be seen in Fig. 3A, water ingestion resulted a significantly greater ΔEGG-3 cpm power compared to Ensure® intake ($P < 0.05$). Similarly, the Δtransfer function magnitude was greater during water ingestion than during Ensure® intake ($P < 0.05$) (Fig. 3B). There was no significant difference between water ingestion and Ensure® intake regarding the change of any HRV parameter.

Discussion

The present study showed that [1] good

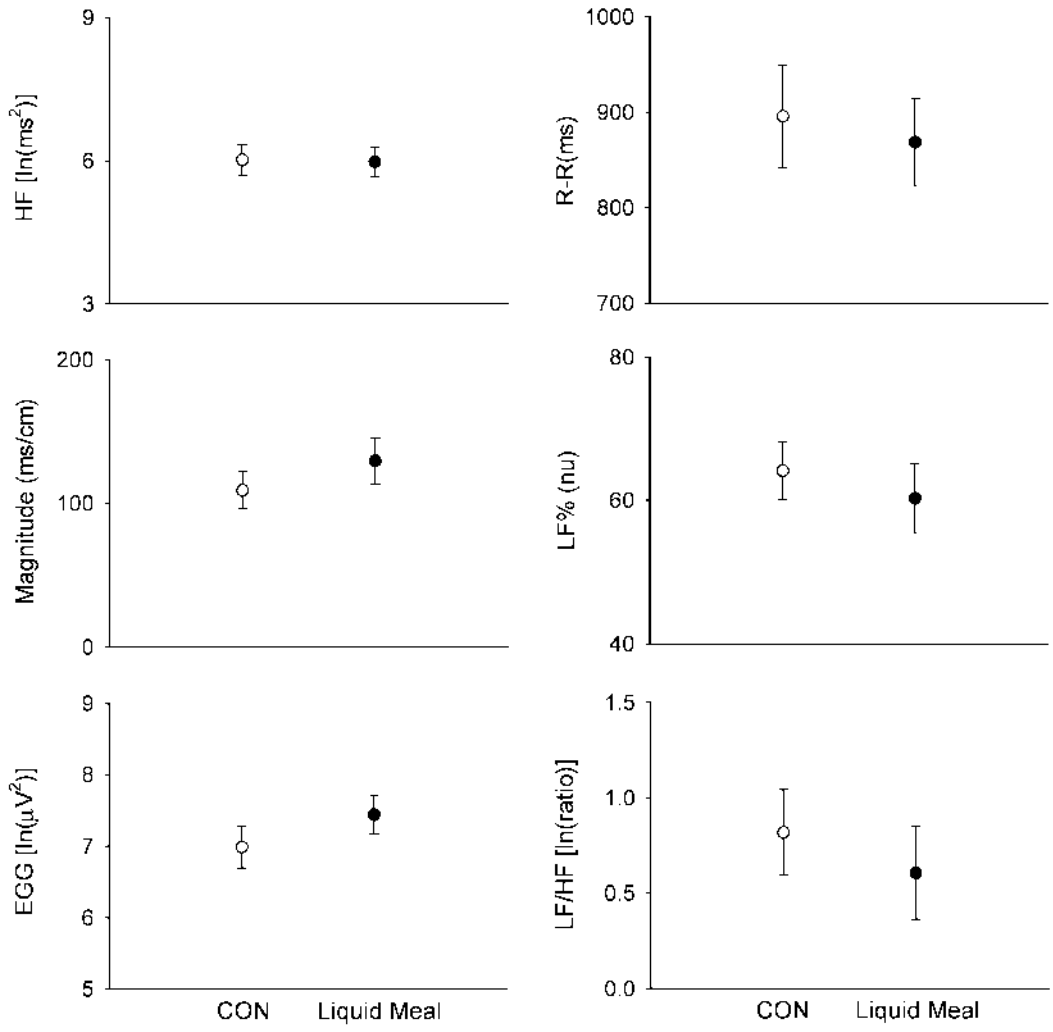

Fig. 2. Changes in high-frequency power of HRV (HF), transfer magnitude (Magnitude). EGG-3 cpm power (EGG), mean R-R interval (RR), normalized low-frequency power of heart rate variability (LF%), and ratio of low frequency power of heart rate variability to HF (LF/HF) before and after liquid meal intake (Ensure®). Ln, natural logarithm. CON, control, *i.e.*, before liquid meal intake. Values are presented as mean ± SEM, n = 16. There were no significant changes in any HRV or EGG variable during the test periods.

coherence between respiration and HRV over ventilatory rates of 0.2-0.4 Hz was seen with Ensure®, [2] there were no significant changes in any HRV and EGG variable including EGG-3 cpm amplitude and the transfer magnitude during Ensure® intake, and [3] water differed from Ensure® in term of the changes of HRV and EGG after gastric stimulation.

By using Ensure®, we have observed a high linearity between variability in respiration and HRV which has previously suggested to be an indicative of the influence of the respiratory pumping mechanism on heart rate fluctuations (4). This notion is in agreement with our previous investigation (4) which has demonstrated the relatively constant magnitude of the transfer function between respiration and HRV signals within physiological range of respiration. Other studies have confirmed that the magnitude characteristics of the respiration to HRV transfer function can be used to assess the role of each branch of the autonomic nervous system (ANS) (3). However, Ensure® did not induce any increase in EGG or cardiac parasympathetic activity as has been shown with water by using transfer function analysis of HRV (4). The lack of the EGG power increase after intake with Ensure® is similar to a previous study by Chen and McCallum who did not observe a postprandial increase in EGG amplitude with milk (6). Our study could extend their findings by showing absence in any increase in the cardiac vagal index as measured by respiratory sinus arrhythmia and the transfer function with Ensure®.

The normal postprandial power increase in the

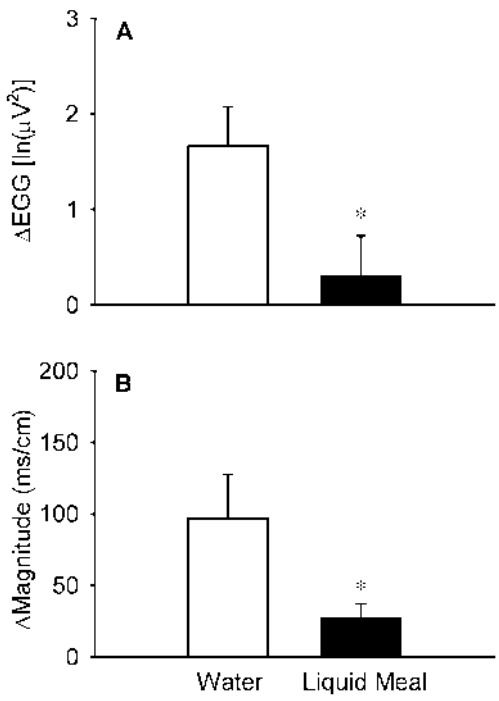

Fig. 3. Difference between the effect of water and a liquid nutritional meal (Ensure(r)). Water ingestion resulted a significantly greater ΔEGG-3 cpm power compared to a liquid nutritional meal (*$P < 0.05$, **A**). Similarly, the Δtransfer function magnitude was greater with water ingestion than with liquid meal intake (*$P < 0.05$, **B**).

EGG signals reflects the increase of gastric electrical activity and contraction. It has been reported that the power increase of EGG is ascribed to the presence of electrical response activity during motor activity (14, 30), or distension which brings the stomach closer to the recording electrodes (5). Studies have shown that food content (size, volume, caloric content, etc.) may influence the postprandial gastrointestional response (17, 27, 31). In the present study, a nutritional liquid meal was chosen as the test meal. Although we have previously shown that water ingestion results in a significant increase in the EGG power (4), it is still a debate regarding the effect of eating on stomach. Previous works demonstrated a good response in postprandial amplitude with liquid meal or yogurt (13, 16). Conversely, another study did not observe such alteration in EGG by using milk as a test meal (6). The difference in the effects on gastric myoelectrical activity between water and liquid meal could be explained by the fact that exposure of the small intestine to fat triggers inhibition of antral contractibility (28). It has been reported that exposure of the small intestine to glucose did not result in an increase in the EGG power (36). Similar results have been demonstrated by Macintosh *et al*. who observed intraduodenal lipid infusion has no effect on EGG power (23). Although we did not directly measure the intraduodenal effect of fat or carbohydrate on EGG, our study would support those findings by showing absence of postprandial alteration in EGG by using Ensure®. It is conceivable that gastric motility depends on the type of food ingested *via* either neural or hormonal mechanisms. Therefore, further study will be needed to evaluate the role of gastrointestinal hormones on EGG associated with Ensure® intake.

In the present study, we found that Ensure® did not provoke a parallel response of the cardiac parasympathetic tone (the transfer magnitude) and the gastric myoeletrical activity (the EGG-3 cpm power). This was reflected by the absence of the postprandial changes in the EGG or HRV variables. Although it may be well tolerated by patients, the liquid meal fails to generate the expected postprandial changes and therefore not suitable for use as a test meal. Motor activity of the stomach, like other gastrointestinal organs, is modulated by changes of vagal activity. An excellent correlation has been demonstrated between the EGG power and the cardiac parasympathetic activity (4, 34). However, another study using a solid meal of 500 Kcal has shown a sustained increase in the postprandial sympathovagal balance (22). The content (volume, composition) might account for the discrepancy in the results. Thus, it is conceivable that the lack of EGG response with liquid meal could be accompanied by absence of the change of the cardiac parasympathetic activity as measured by HRV. In addition, absence of postprandial cardiac parasympathetic increase could be partially supported by the suppressive effect of the decrease in venous return which is secondarily induced by an increase in splanchnic blood flow after a meal (35).

The limitation of this study could arise for the recording length of 10 min which would potentially lead to a bias in pre- and postprandial EGG responses. In a previous study done by Levanon *et al.*, who found the misinterpretation rate of EGG dramatically increased when the recording length was reduced to 15 min (21). In addition, the migration motor complex might influence the results within such a short recording period.

Although there was a good correlation between respiration and HRV over ventilatory rate of 0.2-0.4 Hz in young healthy subjects, the EGG-3 cpm power as well as the transfer function magnitude did not achieve a significant increase after intake with Ensure®. In summary, we have demonstrated that a liquid nutritional meal such as Ensure® differs from water in provoking the postprandial physiological responses. Further studies will be needed in elderly subjects or patients with disorders of autonomic neuropathy in order to determine whether these physiological

responses differ from those in normal young adults, and to assess the impact of different food contents on vagal function measured by transfer function analysis of HRV and EGG.

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