Transfer function analysis of heart rate variability in response to water intake: correlation with gastric myoelectrical activity

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Chen, C. L., H. H. Lin, William C. Orr, Cheryl C. H. Yang, and Terry B. J. Kuo. Transfer function analysis of heart rate variability in response to water intake: correlation with gastric myoelectrical activity. J Appl Physiol 96: 2226–2230, 2004. —We utilized transfer function analysis of heart rate variability (HRV) and respiration to investigate the effect of water intake on gastric myoelectrical activity and its relationship to vagal activity. The electrogastrography (EGG) and HRV were recorded simultaneously before and after drinking 500 ml of water in 10 healthy subjects. We observed good linearity between lung volumes and HRV signals at a ventilatory rate between 0.2 and 0.4 Hz before and after water intake. The EGG power of 3 cycles/min increased remarkably after the water intake. We found that there was a significant increase in the magnitude of the respiration-HRV transfer function after water intake (P < 0.05). The EGG 3 cycles/min power was positively correlated with the transfer function magnitude throughout the study (r = 0.54, P = 0.01). These results confirm that transfer function analysis of HRV sensitively identifies subtle changes in the respiratory sinus arrhythmia that occurs with water intake. The present findings suggest that transfer function analysis of HRV and respiration after water intake can be used to evaluate vagal nervous activity in the human gut.

THE MECHANICAL ACTIVITY OF STOMACH is regulated by gastric myoelectrical activity, which originates at a pacemaker site in the proximal body and propagates aborally to the distal antrum at a frequency of ~0.05 Hz [3 cycles/min (cpm)] (17). The electrogastrography (EGG) is the most widely used technique to record gastric myoelectrical activity. EGG is a noninvasive method used to obtain a cutaneous recording of gastric electrical and mechanical activity from the upper abdominal surface (5, 6). Using spectral analysis of EGG, previous studies (1, 31) have shown its relationship with gastric motor activity. It is well established that the EGG parameters from spectral analysis are frequency, power, and their derivative (5, 31). It is generally accepted that a wave of ~0.05 Hertz represents normal gastric slow wave (1, 31, 33). Many studies have shown a postwar or postprandial increase in EGG power (7, 10, 20). The relative change of EGG power from before to after certain stimulation is thought to be of clinical significance (5, 10) and may correspond to vagal nerve activity. Although there have been a few reports on the relationship between the EGG parameters and autonomic nervous system (ANS) functions (19, 36), it is still a debate whether EGG power is well associated with ANS functions before and after water intake.

MATERIALS AND METHODS

Subjects. The study was performed on 10 healthy, nonsmoking subjects (women/men = 7/3, aged 27.8 ± 6.3 yr) without symptoms or history of gastrointestinal, cardiovascular, or other diseases. Their body mass index was 22.3 ± 1.9 (range from 17 to 29) kg/m². None had any medication for at least 2 wk before the study. The subjects participating in this study were recruited from a university student population and the general public. Subjects fasted for at least 6 h before the experiment. Studies were accomplished with subjects’ written, informed consent and were conducted in accordance with the Helsinki Declaration.

Recordings. EGG and instantaneous chest circumference signals were recorded noninvasively by an integrated EGG machine (3 CPM, Crystal Bay, NV). Two active electrodes were positioned along the antral axis, one midway between the umbilicus and the xiphoid.
process and the other 2–3 cm to the right of the first. A bipolar EGG signal was derived from these two active electrodes. The third electrode was used as an electric ground and placed over the right midaxillary costal margin. The high-cut frequency of the EGG amplifier was 0.3 Hz, and the low-cut frequency was 0.016 Hz. Instantaneous chest circumference signals were used to quantify respiratory movements. A precordial electrocardiogram (ECG) was also taken from each subject by a universal bioelectric amplifier. The high-cut frequency of the ECG amplifier was 16 Hz, and the low-cut frequency was 0.68 Hz. All measurements were performed in the daytime (0800–1600), while each subject laid quietly and breathed normally in a quiet and air-conditioned (25°C) environment. These biological signals were recorded 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 (37°C) in a period of 5 min and then again assumed a supine position. The recording was stopped 30 min after water intake.

Data acquisition and storage. All EGG, chest circumference, and ECG signals were simultaneously and synchronously digitized using a 12-bit analog-to-digital converter (Advantech PCL1815) at a sampling rate of 512 Hz. The acquired data were analyzed online but were simultaneously stored on a hard disk for subsequent offline verification. Signal acquisition, storage, and processing were performed on an IBM PC-compatible computer. The computer program was written in Pascal (Borland Pascal 7.0).

Processing of ECG signal. Preprocessing of the ECG signals was designed according to the recommended procedure (34) and was detailed in our laboratory’s previous investigations (23, 24). In brief, the computer algorithm identified each QRS complex and rejected each ventricular premature complex or noise according to its likelihood in a standard QRS template. The R point of each valid QRS complex was defined as the time point of each heartbeat, and the interval between two R points [the R-R interval (RR)] was estimated as the interval between current and latter R points. In the RR-rejection procedure, a temporary mean and standard deviation of all RR were first calculated for standard reference. Each RR was then validated: if the standard score of an RR value exceeded 3, it was considered erroneous or nonstationary and was rejected.

Average periodogram and cross-spectral analysis of respiration and heart rate signals. The stationary RR were resampled and interpolated at the rate of 16 Hz to provide continuity in the time domain. The sampling rate of respiration signals was also reduced to 16 Hz by a 32-point averaging algorithm. 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 to avoid its contribution to the power of lower frequencies. A Hamming window in the time domain was used to attenuate the leakage effect. Power spectral analysis was accomplished by fast Fourier transform, and average periodograms were generated by averaging the autospectra from six time segments.

Statistical analysis. LF (0.04–0.15 Hz) and HF (0.15–0.4 Hz) of HRV were quantified by integration of its average periodogram in the specified ranges (23). The power of the chest circumference signals in the high-frequency range (0.15–0.4 Hz) was also quantified. The power of EGG between 0.042 and 0.058 Hz (2.5–3.5 cpm) was determined as EGG-3 cpm power. The ratio of EGG-3 cpm power in the postwater state to that in the prewater state was defined as power ratio (PR) (36). Similarly, the ratio of HF in the postwater state to that in the prewater state was defined as rHF. Transfer magnitude of respiration-HRV signal pairs were quantified in the high-frequency range: an oscillating frequency was first defined at which the coherence function exhibited the largest value, then transfer magnitude of the oscillating frequency was selected. This algorithm ensured the highest reliability for quantifying the transfer function (22). All of the measurement values are expressed as means ± SE. Data between groups were compared by Student’s t-test. Correlation was assessed using linear regression analysis. The statistical significance was defined as \( P < 0.05 \).

RESULTS

Changes in indexes of HRV, EGG, and respiration-HRV transfer function. The results of spectral analysis in these parameters are shown in Fig. 1. The autospectrum for respiration exhibited a power density in the frequency range of 0.2–0.4 Hz. Frequency-domain analysis of RR provided a detailed observation of HRV. HF and LF were clearly identified at 0.15–0.4 and 0.04–0.15 Hz, respectively. The coherence function further demonstrated good linearity between respiration and HRV signals at a ventilatory rate between 0.2 and 0.4 Hz before and after water intake. It was also noted that 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 0.0–0.2 Hz throughout the study.

Figure 2 shows the quantitative analysis of HRV, EGG, and respiration-HRV transfer function. We found that there was a significant increase in the magnitude of the respiration-HRV transfer function after water intake \( (P < 0.05) \). The EGG-3 cpm power increased remarkably after the water intake. Although PR was positively correlated with rHF \( (r = 0.56, P < 0.05) \), there was an absence of correlation between EGG-3 cpm power and HF \( (r = 0.05, P > 0.05) \) (Fig. 3A). By contrast, there was a positive correlation coefficient between EGG-3 cpm power and the transfer magnitude throughout the study \( (r = 0.54, P < 0.05) \) (Fig. 3B).
The present study showed 1) that excellent coherence between respiration and HRV over ventilatory rates of 0.2–0.4 Hz was observed, 2) that EGG-3 cpm power and the respiration-HRV transfer magnitude significantly increased after ingestion of water, 3) that there was a positive correlation between the PR and rHF throughout the study, and 4) that there was a positive correlation between the EGG-3 cpm power and the respiration-HRV transfer magnitude from before to after water ingestion.

Our demonstration of maintained high linearity between variability in respiration and HRV is indicative of the influence of the respiratory pumping mechanism on heart rate fluctuations. This notion was further supported by the relatively constant magnitude of the transfer function between respiration and HRV signals within the physiological range of respiration (3). These 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 ANS. Hence, our results suggest that water ingestion increases cardiac vagal activity by using transfer function analysis of HRV. These findings are consistent with the fact that food intake increases the cardiac vagal activity as measured by RSA (35) and by the fact that the increase in postprandial power is not seen after vagotomy (11, 32).

In the present study, water intake produced an increase in HF, although these values did not reach statistical significance. These findings may be explained by the difference of experimental conditions [e.g., case number (type II error), food content, and conditioning of breathing]. Kaneko et al. (19) demonstrated that liquid food intake enhances the cardiac vagal activity (HF component). Our results were consistent with what was found by Watanabe et al. (36), who, using water ingestion, did not show a significant difference in the HF but demonstrated that the change of EGG power (PR) correlated well with the change of cardiac vagal nervous activity (rHF). It is likely that power spectral analysis of HRV is able to reflect the linearity between changes of HRV and gastric myoelectrical activity in response to water intake. Previous studies have demonstrated that the respiration (i.e., rate and tidal volume) parameters modulate the relationships between HF component and cardiac parasympathetic activity (12), and these findings point to the importance of controlling for respiratory parameters when RSA is used as a cardiac vagal index. Our studies also demonstrated a decrease in power density of respiration after water intake. Therefore, it appears to be more reasonable to assess the effect of water intake on cardiac vagal activity by using transfer function analysis of HRV and respiration.

The normal postprandial power increase in the 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 (15, 31) or to distension, which brings the stomach closer to the recording electrodes (4). There have been some controversial results regarding distension. Previous works demonstrated that inflation of an intragastric balloon was associated with increased EGG amplitude in anesthetized dogs treated with glucagon to paralyze the stomach (26). Conversely, sham feeding increases the EGG power transiently without distension of the stomach (32). Previous results have shown that EGG power increased after ingestion of 150 ml of water (36). There is also a report that EGG power decreased on a full stomach after ingestion of water (20). These findings indicate that the volume of water as well as the distension of the stomach may not necessarily reflect the EGG power increase after water intake. In the present study, water intake increased the EGG-3 cpm power and enhanced the cardiac vagal activity (the transfer magnitude) with significant correlation between them. On the basis of the above, our results suggest that drinking water provokes a parallel response of cardiac vagal activity associated with the gastric electrical activity and contraction reflected by EGG power. Hence, the transfer function analysis of HRV and respiration cannot only sensitively detect the changes of HRV but also reflect the linearity between HRV magnitude and EGG power.

The change of cardiac vagal activity after water ingestion may be associated with a change of gastric electrical activity for the following evidence. In the fasting state, the interdigestive motor activity is modulated by the enteric nervous system with gastrointestinal hormones (18, 29), the extrinsic parasympathetic and sympathetic nervous system (37), and the central
nervous system. It has been indicated in the fasted dog that vagal nervous activity is considered to be associated with phasic motility (27). In the fed state, the vagal nerve is thought to mediate the immediate conversion in the gastric motor activity from the fasting pattern to the fed pattern (14). Thus the change of the gastric motor activity from before to after water ingestion may correspond to the change of vagal nervous activity. Furthermore, vagal activity, as assessed by the indirect method of RSA, reflects the vagal influence on the heart. The assumption that RSA activity is representative of vagal activity is supported by the findings reported by Hausken et al. (16).

Efferent impulses from the central vagal nuclei affect an autonomic outflow to the skin and thoracoabdominal viscera, such as the heart, great vessels, and the proximal gut (13).

In conclusion, we have investigated the phenomenon of RSA to understand both the precise relationships between the respiratory function and the heart rate response and how this relationship provides insight into the autonomic functioning involved in the control of heart rate. Using transfer function analysis of HRV, we are able to demonstrate positive correlation between the EGG power and cardiac vagal nervous activity, suggesting that simultaneous recording of EGG, respiration, and ECG signals for transfer function analysis is important to estimate the vagal nervous activity. These findings reemphasize the importance of controlling for respiratory parameters when RSA is used as a cardiac vagal index. Finally,

**Fig. 2.** Changes in respiration (HFResp) and high-frequency power of HRV (HF), respiration-HRV transfer magnitude (Magnitude), EGG-3 cycles/min power (EGG), mean R-R interval (R-R), variance of R-R interval (Var), low-frequency power of HRV (LF), and ratio of LF to HF (LF/HF) before and after water intake. Con, control. Values are presented as means ± SE; n = 10. *P < 0.05.

**Fig. 3.** Relationships between EGG and HF (A) and between EGG and respiration-HRV transfer magnitude (B).
transfer function analysis of HRV and respiration sensitively identifies even the subtle change in autonomic alterations that occur with water intake and consequently should be valuable in assessing autonomic regulation in both healthy individuals and patients with a variety of disorders accompanied with neuropathy.

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REFERENCES