DISRUPTION OF NORMAL GASTRIC MYOELECTRIC FUNCTIONING

Disruption of Normal Gastric Myoelectric Functioning by Sleep

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Study Objectives: The aim of this study was to assess the effects of sleep on gastric myoelectric activity as measured by electrogastrography in healthy individuals. The goal was to elucidate the role of central influences in the regulation of normal gastric functioning.

Design: Electrogastrogram (EGG) was recorded during polysomnographically monitored waking and sleep.

Setting: Sleep laboratory.

Participants: 17 healthy volunteers.

Measurements and Results: EGG parameters were computed for 20-minute segments of pre-sleep waking, stage 2 sleep, stage 4 sleep, and REM sleep using both overall and running spectral analysis of EGG data. The dominant power decreased significantly from waking (31.4 ± 1.4 dB) to all sleep stages (23.1 ± 1.5 dB during stage 2; 24.7 ± 1.4 dB during stage 4; 24.3 ± 1.3 dB during REM sleep). The percentage of 2–4cpm activity decreased significantly during NREM sleep (64.6 ± 7.6% during stage 2 sleep; 57.5 ± 5.5% during stage 4 sleep) compared to its waking value (90.8 ± 3.2%), but not compared to REM sleep (74.1 ± 5.4%). The instability coefficient of the dominant frequency increased significantly from waking (0.19 ± 0.03) to all sleep stages (0.36 ± 0.05 during stage 2 sleep; 0.47 ± 0.05 during stage 4; 0.34 ± 0.05 during REM sleep). No significant differences between the sleep stages were found for any measure.

Conclusions: Sleep is associated with increases in gastric dysrhythmia and instability of the gastric slow wave frequency when compared to waking. These findings suggest that the intrinsic electrical activity of the stomach is significantly influenced by central nervous system mechanisms, and support the notion of a brain–gut axis.

Key Words: Sleep, rapid eye movement sleep, electrogastrogram; stomach; gastric myoelectric activity

INTRODUCTION

ELECTROGASTROGRAPHY IS A NON–INVASIVE method of recording gastric myoelectric activity (GMA) from cutaneous electrodes placed on the abdomen.1 The origins of the gastric slow wave as it is reflected in the electrogastrogram (EGG) have been thoroughly investigated.2 Gastric smooth muscle generate electrical control activity (ECA) and electrical response activity (ERA).1 ECA is an omnipresent periodic change in potential with a frequency of about three cycles per minute (cpm), and controls the frequency and propagation of gastric contractions. While the ECA does not indicate contractile activity, the ERA, or spike potential, reflects phasic contractions of the antrum. The dominant frequency of the EGG signal reflects the fundamental frequency of the gastric ECA. The occurrence of phasic contractions and ERA results in an increase in the amplitude of the EGG signal.1,3 Therefore, the EGG can be used as an indicator of gastric motility.4,5

Although the gastric slow wave originates in gastric smooth muscle, there is evidence of additional regulatory mechanisms, including central nervous system (CNS) and autonomic nervous system (ANS) influences.6–8 However, little is known about the mechanisms mediating CNS influences and the role of the CNS in the regulation of normal GMA. Based on the fact that only 10% of vagal fibers are efferent, it is commonly assumed that the control and regulation of GMA is essentially autonomous.6

The study of GMA during sleep provides a unique method for the investigation of the role of the CNS in the control of GMA. Sleep represents a natural state of cortical deactivation, and the various stages of sleep represent subtle changes in arousal levels.9,10 Several previous studies investigating gastrointestinal activity changes during sleep found decreased small bowel and colonic motility,
with motility indices being inversely related to depth of sleep.\textsuperscript{11,12,13} Castiglione et al. have reported similar results for esophageal motor activity.\textsuperscript{14} However, to our knowledge, only one study has investigated GMA with EGG during sleep. The results of the study, which was performed in our laboratory, suggested a decrease in the dominant power from waking to non–rapid eye movement (NREM) sleep, and a subsequent increase from NREM to rapid eye–movement (REM) sleep in healthy controls.\textsuperscript{15} As this study was limited to assessing EGG dominant power changes only, little is known about the effects of sleep on EGG parameters derived from both overall power spectral analysis and running power spectral analysis. Therefore, the current study was designed to assess the effects of sleep on GMA, as measured by the EGG, in healthy individuals.

\section*{METHODS}

\subsection*{Subjects}

17 healthy volunteers (5 males; 12 females) participated in the study. Subjects were between 22 and 55 years old, with a mean age of 36.2 ± 2.3 years. All participants were of normal weight with a mean body mass index (BMI) of 23 ± 0.8. Subjects were screened for any evidence of gastrointestinal disease, sleep disorders, or medication use during a structured interview which included completion of various questionnaires addressing the frequency and intensity of gastrointestinal symptoms as well as sleep problems. The study protocol was approved by the Institutional Review Board of the Integris Baptist Medical Center of Oklahoma. All participants gave informed written consent prior to entering the study and were paid for their participation.

\subsection*{Data Acquisition}

GMA was measured by recording the EGG signal from surface skin electrodes. Standard electrode positioning included placement of one electrode on the midline of the abdomen midway between the umbilicus and the xiphoid process, positioning of another electrode on the left side of the subject's abdomen approximately 6 cm from the midline at a 45–degree angle, and placement of a reference electrode on the subject's left side approximately 10 cm from the midline below the lowest rib. An ambulatory EGG recording device (Digitrapper EGG, Medtronic–Synectics, Shoreview, MN) with low and high cutoff frequencies of 1 and 18 cpm, respectively, was utilized for recording and amplification of the EGG signal. Installed in the recorder was an analog/digital converter for on–line digitization with a sampling rate of 1 Hz.\textsuperscript{16}  

Standard polysomnographic recordings were used for determination of sleep stages, and were carried out using an Alice 3 Polysomnographic System (Healthdyne, Marietta, GA) which consists of an integrated system of amplifiers and computerized data collection. Four channels of EEG (central channels C3 & C4, occipital channels O1 & O2), two channels of electrooculogram (EOG), one channel of chin electromyogram (EMG), and a single channel of electrocardiogram (ECG) were collected at a sampling rate of 100 Hz and stored on magneto–optical disk. Body position was also recorded. The internal clocks of both the polysomnographic system and the digitrapper were synchronized prior to the beginning of each study.

\subsection*{Experimental Protocol}

Polysomnography and electrogastrography were performed during one night in the sleep laboratory, and included a one–hour pre–sleep wake recording, and approximately seven hours of sleep recording. All subjects refrained from any over–the–counter medication for a minimum of 24–hours prior to the study day, and from caffeine for at least six hours prior to reporting to the lab. They consumed dinner prior to 17:00, after which time they restrained from all food and drink. Subjects reported to the laboratory at 20:30. Upon reporting to the lab, electrodes were applied for EGG and polysomnographic recordings. The wake recording lasted from 22:00 to 23:00. During this period, subjects remained in the supine position and watched television. Subjects were monitored via EEG to ensure wakefulness. The sleep–recording was started at 23:00, and subjects were allowed to sleep spontaneously until 06:00.

\subsection*{Data Analysis}

Polysomnographic recordings were scored according to internationally accepted sleep staging criteria using 30–second epochs.\textsuperscript{17} Twenty–minute segments of EGG data during waking, NREM sleep (i.e., stage 2 and stage 4 sleep), and REM sleep were selected for analysis. The selection of these EGG segments was performed blindly, and was entirely based on polysomnographic data: First, all polysomnographic studies were sleep scored without any access to EGG data. Second, four 20–minute periods of (1) waking, (2) stage 2 sleep, (3) stage 4 sleep, and (4) REM sleep were identified. These segments were chosen based on a number of polysomnographic criteria, which included that they must not be interrupted by any stage shift, movement, or movement arousal, and that the individual must not be in the prone position (i.e., supine, left, or right position were accepted). Lastly, the corresponding EGG tracings, which were time–linked to polysomnographic data, were extracted.

For analysis of the digitized EGG signal, overall spectral analysis and running spectral analysis were performed.\textsuperscript{16,18} While overall power spectral analysis provides global frequency and power information for a specified time segment, running power spectral analysis (i.e.,
minute–by–minute spectra) offers more detailed information regarding subtle and short–lasting variations in the frequency and power of the gastric slow wave. Overall power spectra were computed to determine the dominant frequency and dominant power. The dominant frequency, expressed in cycles per minute (cpm), is defined as the frequency at which the power has a peak value, and reflects the frequency of gastric slow waves. The dominant power is the power at the dominant frequency, and is associated with both the amplitude and the regularity of gastric slow waves.

Running spectral analysis, specifically the adaptive spectral analysis method developed by Chen et al. (1993), was used for qualitative and quantitative analysis of each minute of the 20–minute segments. The percentage of normal slow waves (i.e., 2–4 cpm), the percentage of gastric dysrhythmias (i.e., bradygastria, tachygastria, and arrhythmia), and the instability coefficient (IC) of the dominant frequency (i.e., the ratio between the standard deviation and the mean of the dominant frequency) were computed. The percentage of 2–4 cpm activity represents a quantitative assessment of the regularity of gastric slow waves; conversely, the percentage of gastric dysrhythmias reflects abnormalities in gastric slow wave activity. The instability coefficient of the frequency mirrors subtle, short—lasting variations of the gastric slow wave over a specified time segment.

### Design and Statistical Analyses

The study utilized a repeated measures design, with each subject serving as his or her own control for the dependent measures in order to minimize inter–subject variability. Recordings obtained during four periods were compared: wakefulness, NREM sleep (i.e., stages 2 and 4), and REM sleep. Dependent variables included the dominant frequency, the dominant power, the instability coefficient of the dominant frequency, the percentage of 2–4 cpm activity, and the percentage of gastric dysrhythmias [i.e., bradygastria (0.5–2 cpm), tachygastria (4–9 cpm), and arrhythmia].

For statistical analysis of the dependent measures derived by the EGG, a one–way analysis of variance (ANOVA) was carried out utilizing $\alpha$ set at 0.05. Pairwise multiple comparisons were carried out with $\alpha$–adjustment using Tukey's HSD method. In order to investigate the possible role that body position may have played in the observed dominant power changes, comparisons of the dominant power changes from waking to stage 4 sleep between the supine and the non–supine (i.e., right or left side) body position were carried out. Stage 4 sleep was chosen for the comparison due to the small number of observations in the non–supine positions during the other sleep stages. Of the analyzed time periods, only 5 of 13 individuals were on their left or right sides during stage 2 sleep, and only 3 of 13 participants were on their side during the REM sleep. Body position data were not available for three individuals. All subjects were in the supine position during the wake recording. Comparisons were carried out using a two–independent samples t–test.

### RESULTS

All results are presented as means±SEM (standard error of the mean). Sleep data are shown in Table 1. The results demonstrated that participants slept well—within the expected norms, with a sleep efficiency greater than 85%
and a normal distribution of sleep stages.

Regarding the EGG data, results revealed a number of sleep–related changes. One participant was excluded from further analysis because the waking EGG showed an unusually high percentage of dysrhythmias (i.e., over 50%), which differed by over 2.5 standard deviations from the mean and suggested abnormal gastric functioning. The ANOVA on the dominant power showed a significant main effect ($F(3,45)=15.82; p<.001$). As illustrated in Figure 1, post–hoc comparisons revealed that the dominant power decreased significantly from waking (31.4 ± 1.4 dB) to all sleep stages (23.1 ± 1.5 dB during stage 2, $p<.001$; 24.7 ± 1.4 dB during stage 4, $p<.001$; 24.3 ± 1.3 dB during REM sleep, $p<.001$). There were no significant differences between the sleep stages. Figure 2 shows examples of overall power spectra for one individual during waking and stage 4 sleep (a), and during waking and REM sleep (b).

To assess whether differences in body position played a role in these dominant power changes, the delta scores for the change in dominant power from waking to stage 4 sleep in subjects sleeping in the supine position were compared to the change from waking to stage 4 in those sleeping in the non–supine (i.e., left or right side ) position. There were no significant differences in the delta score for supine and non–supine (0Δ = 6.2 ± 2.9 dB) and non–supine (0Δ = 7.8 ± 1.8 dB) (p=.66) position.

The overall ANOVA on the percentage of 2–4cpm activity revealed a significant effect ($F(3,45)=7.6175; p<.001$). As shown in Figure 3, pairwise multiple comparisons demonstrated that the percent 2–4cpm activity decreased significantly during NREM sleep (64.6 ± 7.6% during stage 2 sleep, $p<.05$; 57.5 ± 5.5% during stage 4 sleep, $p<.001$).
compared to its waking value (90.8 ± 3.2%). There was no significant difference between waking and REM sleep (74.1 ± 5.4%). Figure 4 shows examples of running power spectra of one individual for waking (a) and stage 4 sleep (b).

For dysrhythmias, the ANOVA on the percentage of tachygastria revealed a significant effect (F(3,45)=4.636;p<.05), as did the ANOVA on the percentage of arrhythmia (F(3,45)=2.963;p<.05). Figure 5 illustrates changes in dyrhythmias across states of consciousness, and indicates significant changes during the stages of NREM sleep, but not during REM sleep, compared to waking.

The ANOVA on the instability coefficient of the dominant frequency revealed a significant effect (F(3,45)=9.06; p<.0001). As shown in Figure 6, the instability coefficient increased significantly from waking (0.19 ± 0.03) to all sleep stages (0.36 ± 0.05 during stage 2 sleep, p<.05; 0.47 ± 0.05 during stage 4, p<.001; 0.34 ± 0.05 during REM sleep, p<.05). There were no significant differences between the sleep stages.

There were no significant changes in dominant frequency from waking (2.9 ± 0.1) to sleep (2.9 ± 0.1 during stage 2, 3.0 ± 0.1 during stage 4, and 3.0 ± 0.1 during REM sleep). However, stage 4 was characterized by the absence of a clearly discernible dominant frequency (see Figure 2a for an example) in eight individuals. Absence of a discernible dominant frequency was present in three individuals during stage 2 and four individuals during REM sleep.

**DISCUSSION**

The results of this study demonstrated significant decreases in the dominant power and the percentage of normal 2–4cpm activity during sleep, and these findings were paralleled by significant increases in the instability coefficient of the dominant frequency and the presence of dysrhythmias. The results confirmed that the decrease in the dominant power was not due to changes in body position. Together, these data provide strong evidence of differences between sleep and wakefulness in GMA as reflected by the EGG in healthy individuals. Sleep, particularly NREM sleep, is associated with gastric dysrhythmia and decreased regularity and amplitude of the gastric slow wave.

The results of this study do not support strong differences between the sleep stages on measures of the EGG, as evidenced by the lack of statistically significant differences. However, a closer examination of the data suggests an inverse relation of GMA disruption and depth or synchronization of sleep. The percentage of 2–4cpm activity and the instability coefficient of the frequency revealed maximum dysrhythmia and instability during stage 4 sleep, while values increased during REM sleep to levels intermediate between stage 4 and waking.

This finding is in line with the concept that REM sleep is a period of enhanced cortical arousal (i.e., reduced cortical de–activation), while stage 4 sleep is characterized by maximal cortical de–activation.9,10,22 Thus, the EGG results suggest enhanced GMA synchronization and less dysrhythmia during periods of increased cortical arousal (i.e., waking and REM sleep) and GMA disruption associated with diminished cortical arousal (i.e., stages 2 and 4 of NREM sleep). Together, these findings substantiate the notion of a brain–gut axis reflected in the alteration in normal GMA during periods of diminished cortical arousal.

Previous research from our laboratory has documented a significant increase in the dominant power during REM sleep when compared to NREM sleep.15 The present results did not reveal a similar increase in dominant power during REM sleep despite the fact that there was less dysrhythmia during REM sleep when compared to NREM sleep. Since the dominant power reflects both regularity and amplitude of the gastric slow wave, a decreased amplitude could account for the diminution of the dominant

![Fig. 5](image_url)—Changes in the percentage of dysrhythmias (i.e., bradygastria, tachygastria, arrhythmia) across sleep stages. The percentage of bradygastria was significantly increased during stage 2 sleep (*p<.05) and stage 4 sleep (*p<.05) when compared to waking, and the percentage of arrhythmia is significantly increased during stage 4 sleep when compared to waking (*p<.05).

![Fig. 6](image_url)—Changes in the instability coefficient of the dominant frequency across sleep stages. IC = instability coefficient. The instability coefficient of the dominant frequency was significantly increased during stage 2 sleep (*p<.05), stage 4 sleep (*p<.001), and during REM sleep (*p<.05) when compared to waking.
power during REM sleep.

Lastly, some consideration needs to be given to the possible complications of the relatively short measurement intervals for each state of consciousness (i.e., 20 minutes). In a previous study from our laboratory, Levanon et al. have suggested optimal reliability and predictability of results with a recording length of 30–60 minutes. However, a 15-minute recording interval, while introducing some variability, did not result in a statistically different result on any EGG parameter when compared to 30–60 minute intervals. Given the exigencies of acquiring data from normal sleep which preclude any reasonable possibility of consistently obtaining data segments exceeding 20 minutes in each sleep stage, we feel that the 20-minute recording intervals is the best that can be obtained under sleeping conditions, and that this measurement duration does not appreciably compromise the results of this study.

Conceptually the findings from this study would have to be considered extraordinary, because they challenge the common assumption of an autonomously generated gastric slow wave and the minor status of extrinsic influences. Other support for the mediation of gastric myoelectric activity by the CNS comes from studies investigating the effect of cephalic stimulation on measures of the EGG. These studies revealed an increase in the dominant power following cephalic stimulation. This effect was absent following vagotomy, which led to the conclusions that the CNS does influence GMA, and that this is largely mediated by vagal efferent pathways.

In summary, the EGG results support the concept that CNS mechanisms influence the coordination and regulation of GMA in healthy individuals. Sleep is associated with increased dysrhythmia and instability, and decreased amplitude of the gastric slow wave. These findings lend further support to the notion of a brain–gut axis, and suggest that the concept of the gastric slow wave as largely autonomously generated may have to be further revised.

REFERENCES