Modulation of gastric motor activity by a centrally acting stimulus, circular vection, in humans

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Received 14 September 2000; accepted in final form 6 November 2000

Faas, Henryk, Christine Feinle, Paul Enck, David Grundy, and Peter Boesiger. Modulation of gastric motor activity by a centrally acting stimulus, circular vection, in humans. Am J Physiol Gastrointest Liver Physiol 280: G850–G857, 2001.—The aims of this study were to investigate gastric motor correlates of vection, a centrally acting stimulus, and relate these responses to the induction of motion sickness symptoms. Antral contractile activity and gastric emptying were assessed by magnetic resonance imaging in healthy subjects during two different protocols. Vection was induced by an optokinetic drum, and subjects repeatedly rated the intensity of vection and nausea on 0–10 analog scales. Vection delayed gastric emptying (99% [89–102%] interquartile ranges] of volume retained at 28 min; control situation: 79% [69–81%], P < 0.05). Antral contractile activity during two different protocols. Vection was induced by an optokinetic drum, and subjects repeatedly rated the intensity of vection and nausea on 0–10 analog scales. Vection delayed gastric emptying (99% [89–102%] interquartile ranges] of volume retained at 28 min; control situation: 79% [69–81%], P < 0.05). Antral contractile activity followed a distinct time course of rapid decrease (64% (−72 to −59%) change from baseline activity) immediately after onset of drum rotation followed by gradual recovery upon withdrawal of the stimulus. No relationship was found between the severity of nausea and inhibition of gastric emptying or antral contractile activity. The inhibition of antral contractile activity appears to be a good measure of the peripheral response to vection but is probably independent of subjective symptom induction.

WHILE THE INVOLVEMENT OF THE brain in the control of gastrointestinal motor function has long been appreciated (3, 5, 13, 15, 21), it is now also recognized that the central nervous system plays an important role in conditions such as functional bowel disorders, in which stressful events may alter bowel motor function and in this way trigger gastrointestinal symptoms. Of these symptoms, nausea represents a serious problem in patients suffering from functional dyspepsia (6).

The fact that illusory self-motion (vection) slows gastric emptying (18) and can also elicit nausea may be used to study the effects of this centrally acting stimulus on gastric motor function. This would allow further elucidation of the nature of the accompanying physiological symptoms of motion sickness in relation to changes in gastric function. Gastric emptying, however, is an integrated response to a change in overall gastroduodenal motor function. Therefore, its assessment does not allow more detailed conclusions, particularly on the timing and kinetics of the change with respect to the stimulus. Gastric pacemaker activity as measured in electrogastrography, on the other hand, does not directly translate into motor activity (22). Individual motor components, such as antral contractile activity, may reveal much more precisely the immediate response to a stimulus, providing a directly assessable outcome measure of the peripheral response to a centrally acting stimulus. Observation of gastric contractile activity during experience of vection has been reported using manometry (17). However, interpretation of the manometric data remained difficult, and no simultaneous measurement of gastric emptying was performed. Direct observation of gastric contractile activity with respect to the stimulus could also serve as an objective parameter for the quantification of the timing and kinetics of a specific physiological effect of nausea and illusory self-motion. A technique to achieve this aim is magnetic resonance imaging (MRI), which has recently been developed to assess antral contractile activity and gastric emptying (11, 19).

The aim of our study was to directly assess by MRI the changes in gastric motor activity in response to an external visual stimulus (optokinetic stimulation inducing illusory self-motion) and to relate these changes to symptoms of motion sickness and changes in gastric emptying or antral contractile activity. Our hypothesis was that changes in antral contractile activity closely mirror the presence of the vection stimulus, while gastric emptying is an overall reflection of a change in gastrointestinal motor function.

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METHODS

Subjects

Healthy subjects between 23 and 50 yr (median 25 yr), 12 for part 1 (4 male, 8 female) and 7 for part 2 (4 male, 3 female), participated in the study. The subjects were not taking any medication and had no history of gastrointestinal disease. Smokers were asked to refrain from smoking on the morning before the study. Written informed consent was obtained from the subjects, and the protocol was approved by the ethics committee of the University Hospital Zurich.

Study Design

The study consisted of two parts. In part 1, the general effect of the vection stimulus in a horizontally oriented optokinetic drum (Figs. 1A and 2) on gastric emptying, motility, and symptoms was investigated. In part 2, the focus was on determining the kinetics of the changes in gastric motor activity under vection. To distract the subjects’ attention from the idea that motion sickness symptoms were a focus of the study, the subjects were told that the purpose of the study was to investigate the effect of central nervous system stimulation (by vection) on gastric contractions.

Subjects attended the laboratory after fasting for at least 4 h. After ingestion of 600 ml 15% glucose solution, to which 600 μmol Gd-DOTA (Dotarem; Laboratoire Guerbet, Aulnaysous Bois, France) had been added as a magnetic resonance contrast agent, subjects were placed in the magnetic resonance imager in a supine, 30° right angulated position, and a survey scan was performed. The subjects were positioned such that their entire visual field was covered by the inside of a horizontal optokinetic drum.

Vection Drum

Illusory self-motion was induced by means of a circular vection drum (length: 1 m, diameter: 40 cm) made of magnetic resonance-compatible material and built by modifying a design described previously (8; Fig. 2). Alternating 5.7° black and 9.3° white vertical stripes covered the inner surface. The
drum incorporated a transparent upper end to illuminate the inside of the cylinder and to allow observation of the subjects. In addition, this lid was connected via a shaft to an external motor that rotated the drum in an anti-clockwise direction at a speed of 60°/s. The drum was constructed such that its rotation axis was turned by 90° from an upright position and therefore could rotate around subjects in supine position in the magnetic resonance imager. The subjects were positioned on a padded board in the scanner with their heads and shoulders resting on an extension reaching into the interior of the drum such that the drum ended at shoulder level. The subjects’ faces were aligned with the rotation center of the drum, and their entire field of vision was covered by the drum and, hence, the stripes.

MRI

Volume scan. Intragastric liquid volume was assessed with a previously described method (11). Briefly, a Turbo Spin Echo scan [transverse slice orientation, echo time (TE) = 12 ms, repetition time (TR) = 576 ms, flip angle α = 90°] with 20 contiguous slices (slice thickness: 10 mm) was performed over 60 s. The in-plane resolution was 1.5 mm (matrix size: 256 × 256 pixels, field of view: 380 mm). Scans were divided into four measurement periods of 15 s each, and the subjects were asked to hold their breath during the length of each of these measurements to avoid motion artifacts. Lipid signal suppression was achieved by selective excitation and gradient dephasing before the imaging sequence.

Dynamic scan. Double-oblique dynamic images (see image plane orientation in Fig. 5, inset) were acquired over 120 s (part 1) and 240 s (part 2) with a gradient echo sequence (TE = 7.0 ms, TR = 25.2 ms, α = 20°, in-plane resolution: 2 mm) to assess antral contractile activity with a time resolution of 1 s per image. The subjects were asked to breathe shallowly during image acquisition.

Assessment of Symptoms

Immediately before each volume scan (i.e., after each dynamic scan), subjects were questioned about their experience of symptoms of illusory self motion and nausea and were asked to rate their intensity on a scale from 0 to 10, with 0 indicating “symptom not present” and 10 indicating “symptom most severe.” To distract their attention from nausea, the subjects were also asked to rate the intensity of drowsiness and sleepiness, but these data were not entered in the analysis.

Study Protocol

Part 1. Twelve subjects were studied on two different days after the protocol in Fig. 1B. After ingestion of the liquid meal (10 min), a first volume scan was performed [time (t) = 0 min] to determine the initial amount of liquid in the stomach. A period of 10 min was usually required for correct positioning of the subjects in the scanner. Volume scans were repeated every 7 min until the end of the study period at 49 min. After the volume scans, the contractile activity of the antrum was assessed over periods of 2 min using dynamic scans. On the first occasion, the drum remained still over the entire study period (“off-off”). On the second day (“on-off”), the drum was rotated from the first volume scan at 0 min until 28 min (“on”). Thereafter, the drum was still for the remainder of the study (“off”).

Part 2. On a separate occasion, seven subjects were studied following the protocol shown in Fig. 1C (“off-on-off”) after ingestion of the liquid meal (terminated at t = −5 min). After a baseline period of 20 min with no drum rotation, vection was induced for over 20 min. After removal of the stimulus, the study was continued for a further 20 min. Volume scans were performed at t = −5 min, then at t = 10 min, and repeated every 10 min until t = 50 min. Between these volume scans, contractile activity was assessed over 4-min periods.

Data Analysis

Volume scans. In all 20 slices of each volume scan, the contour of gastric content was identified and outlined by a semiautomated edge detection algorithm. These areas were multiplied by the slice thickness and added to obtain momentary intragastric volume. The lag time was defined as the time that up to 90% of initial gastric content was retained in the stomach. Inhibition of gastric emptying was expressed as the difference of the gastric emptying profiles between vection and the control situation at 28 min (i.e., at the end of the drum rotation period). Differences in gastric emptying between subjects experiencing strong nausea and those who did not were also assessed in this way. For this purpose, subjects were grouped on the basis of their nausea ratings into “strong responders,” with a nausea score ≥4, and “weak responders,” with a nausea score ≤2.

Dynamic scans. From the dynamic magnetic resonance scans, antral contractions were extracted and characterized by their degree of lumen occlusion and frequency. The degree of occlusion of the gastric lumen by a contraction (“contractile strength”) was measured manually and defined as the smallest distance between opposite sides of the gastric wall in the contracted state vs. the uncontracted state. The data were expressed as percentage of lumen occlusion, and the mean occlusion per minute was calculated. The frequency was obtained by counting the number of contractions passing over the distal stomach per minute. Analysis of the dynamic scans was carried out by an independent person not involved in the study. In part 2 of the study, the mean degree of lumen occlusion was analyzed in the following three blocks: 4–7 min (baseline); 24–27 min (vection); 54–57 min (recovery).

Relationship between objective measures (gastric emptying and antral motility) and nausea. Correlations were performed to determine possible relationships between gastric emptying (volume retained at 28 min) and subjective symptoms of nausea in all subjects, but also in the strong responders separately. The relationship between the inhibition of antral contractile activity (expressed as the change in lumen occlusion of gastric contractions between on and off periods in the vection condition) and nausea was also examined.

Statistical Analysis

Data are expressed as medians (interquartile ranges). Wilcoxon rank-sum test was used to test for statistical significance. P < 0.05 was regarded as statistically significant. For comparison of unpaired subgroups in part 1, a Mann-Whitney U-test was used. To test for differences in contractile activity at the three time points chosen in part 2 (baseline, vection, recovery), a Friedman test was performed. Relationships between symptom scores and motor parameters were calculated using Pearson’s correlation, stating the correlation coefficient r² and assuming P < 0.05 to indicate a significant linear relationship.
RESULTS

Part 1: Vection (on-off) vs. control (off-off)

Symptoms. Illusory self-motion was experienced with moderate intensity [maximum score: 6 (4.0–6.3)] by all subjects during the vection period subsiding with removal of the stimulus (Fig. 3, left). Seven subjects with a nausea score ≤2 [2 (0–2)] were classified as weak responders, whereas five subjects with a nausea score ≥4 [7 (5–8)] were classified as strong responders (Fig. 3, right). One subject had a maximum score of nine, which in that case led to early withdrawal of the stimulus.

Gastric emptying. MRI scans to assess gastric emptying (transverse slice orientation) could be analyzed from all 12 subjects. Gastric emptying during vection and control situation is shown in Fig. 4. Without the vection stimulus, gastric emptying followed a curvilinear pattern. Vection significantly delayed gastric emptying in 11 out of 12 subjects, with 99% (89–102%) of volume retained in the stomach at 28 min (end of stimulus) compared with 79% (69–81%) in the control situation ($P = 0.019$). There was no difference in gastric emptying during vection between strong and weak responders [volume retained at 28 min; strong responders: 102% (102–106%), weak responders: 96% (88–99%); $P = 0.062$; Mann-Whitney $U$-test]. Vection prolonged the lag time of gastric emptying [vection: 35 min (21–49 min), control: 7 min (5–9 min); $P = 0.029$]. No correlation was found between the severity of nausea, expressed as a maximum score, and the inhibition of gastric emptying, expressed as the difference in volume emptied at $t = 28$ min, neither in all subjects ($r^2 = 0.02, P = 0.68$) nor in the strong responders alone.
Antral contractile activity. Contractile activity (Fig. 5) could consistently only be followed in 10 of 12 subjects, for reasons of image quality, in particular motion artifacts, and failure to find a suitable scan plane (planned on the survey and the transverse scans) within the time frame allocated for this task by the study protocol. Under vection, a significant difference of 19% (12–37%) in the degree of lumen occlusion of the contractions was observed between on and off periods [lumen occlusion; on: 23% (7–41%) vs. off: 35% (15–48%); \( P = 0.008 \)], whereas no difference was found between the two periods in the control situation [change in degree of lumen occlusion: 1% (–27–9%), \( P = 0.799 \)]. No significant correlation was found between the severity of nausea and the inhibition of antral contractile activity (expressed as difference between on and off periods during vection; \( r^2 = 0.15, P = 0.298 \)). During vection, the contraction frequency was 2.4 min\(^{-1}\) (1.5–2.3 min\(^{-1}\)) compared with the same period in the control situation [2.8 min\(^{-1}\) (2.5–3.0 min\(^{-1}\); \( P = 0.051 \)]. After vection, frequency was 2.4 min\(^{-1}\) (2.4–2.8 min\(^{-1}\)) compared with 2.9 min\(^{-1}\) (2.5–3.0 min\(^{-1}\)) during the control situation (\( P = 0.069 \)).

Part 2: Off-On-Off

Symptoms. Although all subjects experienced vection [maximum score 8 (6.5–8.0)], only three out of seven reported symptoms of nausea [peak score 0 (0–1.5)].

Antral contractile activity. Magnetic resonance images could be analyzed from all seven subjects. After onset of the stimulus, a rapid decrease in lumen occlusion of antral contractions was observed (Fig. 6), reaching a maximum change from baseline of –64% [(–72 to –59%) \( P < 0.05 \)] at \( t = 26 \) min (22–27 min), i.e., 12 min after onset of the stimulus. Recovery of contractile activity upon withdrawal of the stimulus (at \( t = 35 \) min) started only after a delay. Antral lumen occlusion remained below –20% change from baseline until \( t = 35 \) min (35–51 min) before returning to levels no longer different from baseline [lumen occlusion, vection (24–27 min): –56% (–62 to –52%); recovery after vection (54–57 min): –6% (–22 to –8%), \( P = 0.018 \), Friedman test \( P < 0.005 \)]. As in part 1, illusion of self-motion commenced immediately [within 47 s (37–51 s), \( n = 6 \), not assessed in one subject] after onset of drum rotation and was maintained at a constant level throughout the vection period, whereas nausea was a gradually increasing sensation. Therefore, the inhibition of antral activity followed the onset of vection more than the onset of nausea.

DISCUSSION

We demonstrated in this study that antral contractile activity is inhibited by optokinetic stimulation and follows a distinctive time course with respect to the stimulus, characterized by a rapid decrease with the onset and a delayed return to baseline after withdrawal of the stimulus. However, the changes in gastric contractile activity did not directly relate to the intensity of motion sickness symptoms.

To accomplish a comprehensive characterization of the effect of vection on the stomach, it is crucial to identify parameters that correspond to changes in physiology in response to the provocative stimulus. Quantification of gastric peristaltic contractions has a number of advantages over the assessment of more complex functions, such as gastric emptying. A delay in gastric emptying, as also shown in this study, takes...
considerable time to develop, whereas the response of antral contractility to the stimulus is immediately apparent. This is especially important when aiming to correlate centrally perceived symptoms and peripheral effects. Because the development of motion sickness is a continuous, dynamic process, it is important to describe the time course of accompanying physiological changes.

The mechanisms underlying the physiological effects and symptoms associated with illusory self-motion and motion sickness are still unclear. The immediate response of antral motor activity to the external stimulus indicates mediation through nervous pathways. Removal of the stimulus was associated with gradual recovery to baseline. To find possible motor correlates, we assessed symptoms of motion sickness in our study at regular intervals and in close temporal association with measurements of gastric emptying and antral contractile activity. Although the effect on antral contractions consistently occurred as an immediate response to the stimulus per se, symptoms developed in some subjects to varying degrees, but were absent in others, and thus did not reflect these changes in antral motor function. These findings support the hypothesis that the symptoms of motion sickness and the changes in gastric function occur independently of each other (4, 17, 18). Studies using electrogastrography (EGG) recordings have led to the conclusion that afferent information from the gastrointestinal tract causes the centrally generated symptom of motion sickness (10). This view has, however, been challenged by other studies that were not able to fully reproduce the EGG findings and suggested the possibility that changes in gastric motor function were an epiphenomenon of nausea induced by vection rather than its cause (17, 18). These observations support our own data, also showing strong peripheral responses (inhibition of antral contractile activity) in the absence of nausea. In accordance with our present data, a recent study in a cat model has also led the authors to the conclusion that physiological responses such as motor and myoelectrical activity accompany motion sickness, but that motion sickness is independent of these physiological changes (12). Although in animals the autonomic responses can be assessed more precisely and in more detail than in humans, the subjective feeling of nausea, the most prominent and relevant symptom of motion sickness, can only adequately be investigated in humans. To link findings from the animal model to studies in humans, the identification of physiological autonomic parameters as shown in the present study with gastric motility is important. The fact that the data from the animal study are in agreement with our findings in humans demonstrates that gastrointestinal motility represents a particularly useful and sensitive autonomic index of motion sickness (12).

It is not entirely clear how gastric electrical activity translates into contractile activity. Studies using intraluminal manometry have shown an absence of detectable contractions during gastric myoelectrical arrhythmias and tachygastria in the EGG (22). We observed a reduction in the strength and frequency of the contractions during vection that may correspond to the observed EGG changes. However, it is unknown why EGG changes can be related to the occurrence of nausea, although this does not appear to be the case with contractile activity. It remains a future task to identify the exact nature of the relationship between contraction frequency and amplitude on the one hand and EGG frequency and power on the other, since intraluminal manometric recording is not able to resolve this in the case of weak, non-lumen-occluding contractions, which may remain undetected (22). In contrast, MRI can reveal gastric contractions of any
degree of lumen occlusion. MRI has another important advantage over manometry, which is particularly relevant when studying the relationship between contractile activity and nausea. Nasogastric intubation itself can, by virtue of the stimulation of the pharynx, induce nausea, which is obviously not desirable in studies of this kind.

The degree of peripheral motor changes observed in our study was probably also influenced by the meal used. The presence of nutrients in the upper gastrointestinal tract has been shown to modulate antral contractile motility, resulting in a slowing of gastric emptying (7). In a previous study using a nutrient-free liquid meal to investigate gastric emptying changes under vection, gastric emptying was much faster in the control situation than in the present study (18). On the other hand, a fat-containing meal emptied significantly slower (4). Therefore, it is likely that in the present study the observed differences in the emptying rates and the contraction amplitudes would have been even greater (due to the reduced feedback inhibition) had a low-nutrient/nutrient-free meal been used. Then, however, the observation time would have been much reduced because of the faster gastric emptying.

To suffice the MRI environment, in which subjects cannot be studied in an upright, seated position, we constructed a horizontal optokinetic drum. Subjects thus experienced the illusion of rolling rather than spinning self-motion, and this might represent a very different stimulus. However, we found the stimulus to be very potent in inhibiting gastric emptying and contractile activity and in inducing vection and motion sickness. Whether the effects were as strong as the effects observed in previous studies (10, 14, 18, 20) cannot be determined due to differences in the rating scales employed. In our present study, we used analog scales with only a few items, enabling us to obtain multiple symptom ratings from the subjects and in this way characterize the development of symptoms throughout the drum rotation period. Other studies employed an elaborate nausea questionnaire, but subjects only rated their symptoms before and at the end of the drum rotation period (14). Because of these differences in the methods of symptom assessment, comparisons between studies have to be made with care.

Because vection is a stimulus acting on the central nervous system and because information on changes in peripheral function from the gastrointestinal tract, but also from the vestibular and visual systems, is transmitted to and integrated in the brain, it is conceivable that there is a common, central mechanism leading to the great variety of effects observed under vection. The only report on central processing of a vection stimulus showed that there is a bilateral activation of the parieto-occipital visual area but also deactivation of the parieto-insular vestibular cortex (2). The authors found a positive correlation between the perceived intensity of circular vection and the relative changes in cerebral blood flow in parietal and occipital areas. They concluded that a “reciprocal visual-vestibular interaction” acts as a multisensory mechanism for self-motion perception, shifting the dominant sensorial weight from one sensory modality to the other. These authors did, however, not allow the visual-vestibular conflict to develop into nausea. According to Reason’s sensory mismatch model (16), incoming signals that create a sensory conflict trigger central mechanisms that mediate the symptoms and physiological correlates of motion sickness. It remains to be investigated further, whether “reciprocal inhibition” is the central mechanism by which sensory conflict is resolved and whether nausea development is the result of a failure to initiate such counterbalance measures.

In summary, we have demonstrated a consistent antral motor response to circular vection that occurs independent of the development of motion sickness symptoms. This gastric motor response represents an objective physiological parameter that can be used to investigate the development of the autonomic response during visual-vestibular conflict. However, it appears that antral contractile activity does not represent a suitable predictor of an individual’s susceptibility to symptoms of motion sickness.

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