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# Effects of ginger on motion sickness and gastric slow-wave dysrhythmias induced by circular vection

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**Lien, Han-Chung, Wei Ming Sun, Yen-Hsueh Chen, Hyerang Kim, William Hasler, and Chung Owyang.** Effects of ginger on motion sickness and gastric slow-wave dysrhythmias induced by circular vection. *Am J Physiol Gastrointest Liver Physiol* 284: G481–G489, 2003; 10.1152/ajpgi.00164.2002.—Ginger has long been used as an alternative medication to prevent motion sickness. The mechanism of its action, however, is unknown. We hypothesize that ginger ameliorates the nausea associated with motion sickness by preventing the development of gastric dysrhythmias and the elevation of plasma vasopressin. Thirteen volunteers with a history of motion sickness underwent circular vection, during which nausea (scored 0–3, i.e., none to severe), electrogastrographic recordings, and plasma vasopressin levels were assessed with or without ginger pretreatment in a crossover-design, double-blind, randomized placebo-controlled study. Circular vection induced a maximal nausea score of 2.5 ± 0.2 and increased tachygastric activity and plasma vasopressin. Pretreatment with ginger (1,000 and 2,000 mg) reduced the nausea, tachygastria, and plasma vasopressin. Ginger also prolonged the latency before nausea onset and shortened the recovery time after vection cessation. Intravenous vasopressin infusion at 0.1 and 0.2 U/min induced nausea and increased bradygastric activity; ginger pretreatment (2,000 mg) affected neither. Ginger effectively reduces nausea, tachygastric activity, and vasopressin release induced by circular vection. In this manner, ginger may act as a novel agent in the prevention and treatment of motion sickness.

treatment; vasopressin

NAUSEA ASSOCIATED WITH MOTION SICKNESS is unpleasant. Current antimotion sickness medications, including antimuscarinics and antihistamines, produce incomplete symptom control and elicit significant side effects such as dry mouth, lethargy, and drowsiness. Ginger, a traditional Chinese herbal remedy for motion sickness, has been used to reduce the nausea and emesis caused by pregnancy (1), chemotherapy (25), and postoperative ileus (3). This herb is increasingly used as an alternative medicine (5), in part because its side effects are minimal. However, its efficacy remains controversial (6). Furthermore, the mechanisms responsible for ginger's antimotion sickness action are not well understood.

In 1982, Mowrey and Clayson (23), using a rotating chair to evoke motion sickness, showed ginger's superiority to dimenhydrinate and placebo in reducing motion sickness. Subsequently, Stewart and colleagues (28), who counted the number of head movements tolerated by healthy subjects sitting in a rotating chair, reported that ginger had little or no protective effect on experimentally induced motion sickness. Their research also showed that, in contrast to the observed effect on nausea, ginger partially inhibited tachygastria induced by circular vection, supporting earlier research implicating tachygastria in the pathogenesis of motion sickness (27).

The sensation of nausea due to motion involves complex neural interactions between the central nervous system and the gastrointestinal tract. Because the subjective symptoms of nausea cannot be evaluated in animals and because the neurotransmitters involved in nausea have many interspecific differences, circular vection, a stimulus that produces the illusion of self motion, has been used to study motion sickness in humans (27).

Gastric dysrhythmias, as induced by circular vection, have been implicated in the pathogenesis of motion sickness (17, 27). We and others (14, 18, 33) have shown that vasopressin released from the neurohypophysis may mediate nausea, because elevated plasma vaspopressin levels demonstrate a close temporal relationship with the development and resolution of nausea evoked by circular vection. Furthermore, selective vasopressin antagonists abolish symptoms of motion sickness in primates (4). We therefore hypothesize that ginger ameliorates nausea induced by circular vection by preventing the development of gastric dysrhythmias and the increase in plasma vasopressin levels. To test this hypothesis, we obtained simultaneous electrogastrographic (EGG) recordings and plasma vasopressin measurements in healthy subjects

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undergoing circular vection with and without pretreatment with ginger in a double-blind, randomized, placebo-controlled study.

## MATERIALS AND METHODS

### *Study Population*

Eighteen healthy volunteers with a history of motion sickness induced by automobile, boat, or airplane travel (8 men, 10 women; aged 18–40 yr) were recruited through a campus-wide advertisement. These volunteers had no history of gastrointestinal disease or gastrointestinal surgery and were taking no medications. Subjects with systemic neurohormonal diseases and those who were pregnant were excluded. Before enrollment in the study, each subject underwent circular vection to determine individual motion sickness susceptibility. Of the 18 subjects, 13 developed moderate to severe nausea within 15 min of vection induction. These 13 were included in subsequent studies to evaluate the effect of ginger on vection-induced nausea and gastric dysrhythmias. Of these 13 subjects, four also participated in the study involving vasopressin infusion with and without ginger pretreatment. All studies were approved by the University of Michigan Institutional Review Board. Informed written consent was obtained from all subjects.

### *Cutaneous Electrogastrography*

Cutaneous EGG was performed according to the method of Stern and colleagues (27). After gentle skin abrasion to enhance electrical conduction, four Ag-AgCl electrodes (Accutac diaphoretic electrocardiogram electrodes; NDM, Dayton, OH) were affixed to the abdomen. The first electrode was placed on the midclavicular line below the left costal margin. The third electrode was placed midway between the xiphoid and the umbilicus. The second electrode was placed equidistant between the first and third electrodes. A fourth reference electrode was affixed to the right upper quadrant of the abdomen. The electrodes were connected via direct nystagmus couplers (model 9859; SensorMedic, Anaheim, CA) to a chart recorder to obtain a continuous display of slow-wave activity. The time constraint was set at 10 s, and the high-frequency cutoff was set at 0.3 Hz to minimize interference from nongastric signals. Respirations were monitored by a belt pneumograph connected to an indirect blood pressure coupler (model 9863B; SensorMedic).

Power spectral analysis was performed across the frequency range from 1 to 9 cycles/min (cpm) on 256-s recording segments in a 76% overlapping fashion using custom-designed software incorporating fast Fourier transform and running spectral analysis. A frequency $\geq$2 and $\leq$4.5 cpm was defined as normal. Tachygastria was defined as $\geq$4.5 and $\leq$9 cpm, and bradygastria was defined as $\geq$1 and $\leq$2 cpm. Frequencies $\leq$1 cpm were not analyzed, because convincing waveforms were not observed below this frequency, nor has bradygastria in humans been reliably characterized in this range (32). Signal powers in the bradygastric, normal, and tachygastric frequency ranges were summed and divided by the sum of the signal powers from 1 to 9 cpm. Bradygastric, normal, and tachygastric activities were expressed as a percentage of total signal power.

### *Circular Vection Studies*

Circular vection was performed using a modification of the methods of Stern and colleagues (27). After an overnight fast, volunteers ingested a 1,000-kcal mixed solid-liquid meal: bacon and cheese sandwich on buttered white bread, scrambled eggs, milkshake, and water (25% protein, 30% carbohydrate, 45% fat). At 30 min postprandial, a subject was seated in the center of a drum (diameter, 76 cm; height, 92 cm), the interior of which was painted with alternating black and white 3.8-cm vertical stripes. The subject's head was rested on a chin rest to maintain head position and minimize visual and auditory distractions. After a basal 15-min EGG recording period, the drum was rotated clockwise at 60°/s for 15 min or until the subject reported severe nausea. After cessation of drum rotation, the subject remained in the drum for 15 min while EGG recording continued.

Subjects were asked to report the first sensation of nausea and to describe the nausea as mild, moderate, or severe. A nausea score quantitated symptom severity: 0 = no nausea, 1 = mild nausea, 2 = moderate nausea, and 3 = severe nausea with impending vomiting. If severe nausea was reported, drum rotation was immediately stopped. The time to the first perception of mild nausea, the latency before the onset of gastric dysrhythmia after vection initiation, and the duration of dysrhythmia after vection cessation were recorded. Subjects were asked to evaluate the severity of nausea at 0, 15, 30, 45, 60, 120, 180, and 240 min after vection cessation by answering a 10-cm visual analog scale questionnaire.

It is known that healthy persons may develop a tolerance to repeated exposure to motion stimuli with a resultant decrease in motion sickness susceptibility (26). Thus individual circular vection studies under each of the test conditions were performed on different days separated by at least 3 days. This protocol has been shown in our laboratory to prevent desensitization to the gastric dysrhythmic and symptomatic effects of circular vection.

Subjects ingested 1,000- or 2,000-mg ginger capsules (Nature's Way, Springville, UT) or a placebo (starch) of identical appearance with 100 ml of water 1 h before circular vection studies were initiated. Tests were performed in a randomized, double-blinded, crossover fashion. Ordering of the different experiments was random to ensure that sequential exposure to drum rotation did not introduce a consistent bias in the results of these investigations. Scoring of nausea symptoms and EGG recording were performed before, during, and after vection, as previously described.

For all circular vection studies, an 18-gauge intravenous catheter was placed in an antecubital vein 30 min before basal recording to determine plasma vasopressin levels. Catheter patency was maintained by slow infusion (60 ml/h) of 0.9% normal saline. Venous blood samples were obtained immediately before drum rotation was initiated and immediately after drum rotation was stopped.

### *Vasopressin Infusion Studies*

Because vasopressin may contribute to vection-induced nausea and slow-wave disruption (14), we studied the inhibitory effects of ginger on the release or action of vasopressin. An 18-gauge intravenous catheter was placed in an antecubital vein for blood sampling. EGG recording was performed on supine subjects in a warm quiet room. Subjects were asked to report the perception of nausea and to grade nausea on a scale of 0–3 (as previously described). If severe nausea with impending vomiting was reported, vasopressin infusion was immediately terminated. Pulse, blood pressure, electrocardiographic activity, and oxygen saturation were monitored throughout the infusion.

On 2 separate days, at least 3 days apart, subjects ingested a ginger capsule (2,000 mg) or placebo 1 h before the basal

EGG recording. A 30-min basal EGG recording began 30 min after completion of a 1,000-kcal mixed solid-liquid meal (see *Circular Vection Studies*). After the 30-min basal EGG recording period, vasopressin was infused at 0.1 U/min iv for 30 min, then at 0.2 U/min infusion for 30 min or as tolerated. EGG recording continued for another 30 min after the infusion was stopped. Tests were randomized, double-blinded, crossover design.

For all vasopressin infusion studies, venous blood was sampled at 15 and 25 min during the basal period and at 15 and 25 min after the initiation of each vasopressin dose or at the report of severe nausea, which necessitated termination of the infusion. Vasopressin levels determined under basal conditions were pooled for each study to provide single values for comparisons between subjects. Similarly, mean stimulated vasopressin levels were obtained by pooling values obtained during vasopressin infusions. There were no significant differences in vasopressin levels at 15 and 25 min, suggesting that steady-state plasma levels were rapidly achieved.

### *Plasma Vasopressin Determination*

The blood samples were immediately centrifuged, and the plasma was frozen and stored at −80°C. The plasma vasopressin level was measured by a specific double antibody radioimmunoassay using $^{125}$I-labeled vasopressin (ALPCO, Windham, NH) as the standard, according to a previously described method (7). Briefly, phosphate buffer (250 ml, pH 7.4) was added to a 400-μl plasma sample. Vasopressin antiserum (50 μl) was added, and the samples were centrifuged and incubated for 24 h at 2–8°C. Vasopressin tracer (100 μ1) was added to each sample, and the samples were centrifuged and incubated for 24 h at 2–8°C. Vasopressin solid-phase second antibody (100 μl) was then added to each sample, and the samples were centrifuged and incubated for 20 min at room temperature. Finally, deionized water (1 ml) was added to each sample, the samples were centrifuged for 5 min at 1,000 *g*, and the precipitates were counted in a gamma counter for 1 min. The sensitivity of the assay was 0.6 pg/ml, and the intra- and interassay coefficients of variation were 1.3–8.5% and 5.0–18.2%, respectively.

### *Statistical Analysis*

All results are expressed as means ± SE. Nausea scores, EGG parameters, and plasma vasopressin levels were compared using two-tailed Student's *t*-tests for paired and unpaired observations. The effects of ginger (1,000 and 2,000 mg) on vection- and vasopressin-induced nausea scores, EGG parameters, and plasma vasopressin levels were compared with two-way ANOVA with employment of Bonferroni corrections for multiple statistical comparisons within the data sets. $P < 0.05$ defined statistical significance.

## RESULTS

### *Circular Vection Studies*

*Effects of ginger on vection-induced nausea.* Of 18 healthy subjects with a prior history of motion sickness, 13 developed nausea during 15 min of circular vection. The maximal nausea score in the control study was 2.5 ± 0.2. Ginger pretreatment (1,000 and 2,000 mg) significantly reduced the maximal nausea score to 1.7 ± 0.3 and 1.8 ± 0.2, respectively ($P < 0.05$; Fig. 1*A*). Latency before nausea onset was 5.6 ± 0.6 min. Ginger (1,000 and 2,000 mg) prolonged latency to 8.5 ± 1.1 and 9.7 ± 1.1 min, respectively ($P < 0.05$; Fig. 1*B*). Moreover, under control conditions, subjects taking placebo took up to 60 min to become asymptomatic after drum rotation ceased (as evaluated by visual analog scale). Ginger significantly reduced the severity of nausea up to 45 min after cessation of circular vection (Fig. 1*C*). There was no difference between the effects of 1,000 or 2,000 mg ginger in reducing nausea, prolonging latency before nausea onset, or in recovery from nausea after vection cessation.

*Effects of ginger on vection-induced gastric dysrhythmias.* Figure 2*A* shows a typical EGG signal response to circular vection during control conditions. Before drum rotation, the gastric slow wave was regular at ~3 cpm. Soon after drum rotation began, the dominant frequency was lost and mild nausea developed. The slow wave became chaotic, and signal activity increased to 4.5–9 cpm, consistent with tachygastria (Fig. 2*B*), and moderate-to-severe nausea developed. With ginger pretreatment, the slow wave remained relatively stable at 3 cpm during circular vection and nausea was not reported (Fig. 3).

The percentage of signal in each of the three frequency ranges was measured to determine the magni-

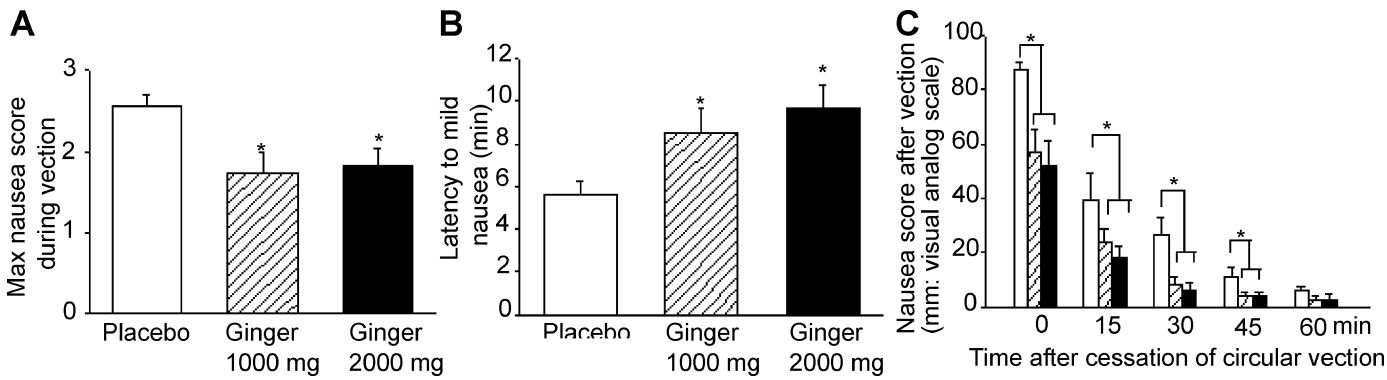


Fig. 1. Effects of ginger on nausea induced by circular vection. *A*: administration of ginger [1,000 mg (hatched bars), 2,000 mg (filled bars)] blunted the maximal nausea score. Ginger also prolonged latency before vection-induced nausea (*B*) and blunted vection-induced nausea at all time points up to 45 min after vection cessation (*C*), compared with control (open bars; *$P < 0.05$). All results are means ± SE ($n = 13$).

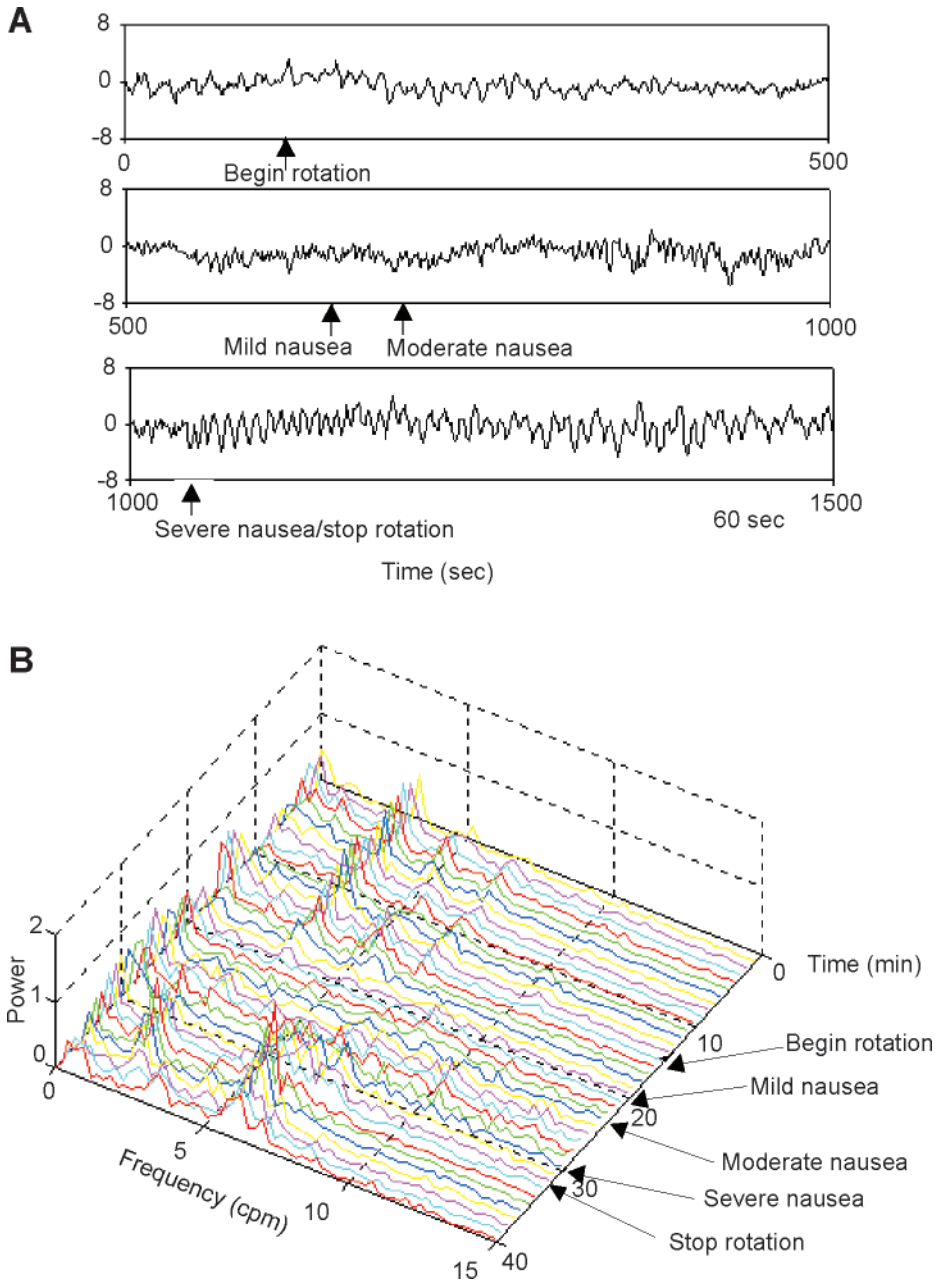


Fig. 2. Raw electrogastrographic (EGG) signals and running spectral analysis of waveform measured while a subject underwent circular vection under control conditions. *A*: the slow wave exhibited an oscillation of 3 cycles/min (cpm) at basal. At 540 s after initiation of drum rotation, the subject reported mild nausea, which was preceded by slow-wave disruption. At 850 s after vection was initiated, severe nausea developed accompanied by tachygastria. Tachygastria persisted after vection cessation. *B*: spectral analysis of the raw EGG signal. Before vection, the slow wave exhibited a dominant frequency of 3 cpm. During vection, 3 cpm were lost associated with a gradual increase in signal activity in the tachygastric range, particularly at 6 cpm; the severity of nausea increased concurrently in this period.

tude of tachygastric, bradygastric, and normogastric activities that developed before, during, and after circular vection. The chaotic slow-wave activity during circular vection often did not exhibit a single dominant frequency. Tachygastric activity significantly increased during vection, compared with basal (28.9 ± 2.8 vs. 16.5 ± 2.3%; $P < 0.05$). Ginger at doses of 1,000 and 2,000 mg significantly reduced tachygastric activity to 21.4 ± 2.0 ($P < 0.05$) and 20.5 ± 3.3% ($P < 0.05$), respectively (Fig. 4*A*). The signal fraction in the bradygastric frequency range did not change during circular vection. Under control conditions, normal rhythmic activity (2–4.5 cpm) was significantly reduced during vection compared with basal (52.2 ± 3.3 vs. 70.0 ± 3.8%; $P < 0.05$) and only partially recovered after vection ceased (60.3 ± 4.0%; $P < 0.05$, compared with baseline). Ginger at 1,000 and 2,000 mg significantly increased normal gastric rhythmic activity during vection [60.6 ± 3.5 ($P < 0.05$) and 63.1 ± 3.1% ($P < 0.05$), respectively, compared with control].

Tachygastria developed during circular vection before the onset of nausea. Under control conditions, latency between the initiation of drum rotation and the development of tachygastria was 3.1 ± 0.9 min. Administration of ginger (1,000 and 2,000 mg) significantly prolonged latency to 7.6 ± 1.7 ($P < 0.05$) and 7.9 ± 1.1 min ($P < 0.05$), respectively (Fig. 4*B*).

Tachygastria persisted 10.4 ± 1.0 min after the cessation of drum rotation. Ginger (1,000 and 2,000 mg) significantly reduced the duration of tachygastria to 4.4 ± 0.3 ($P < 0.05$) and 4.6 ± 0.4 min ($P < 0.05$), respectively (Fig. 4*C*). Thus ginger pretreatment effec-

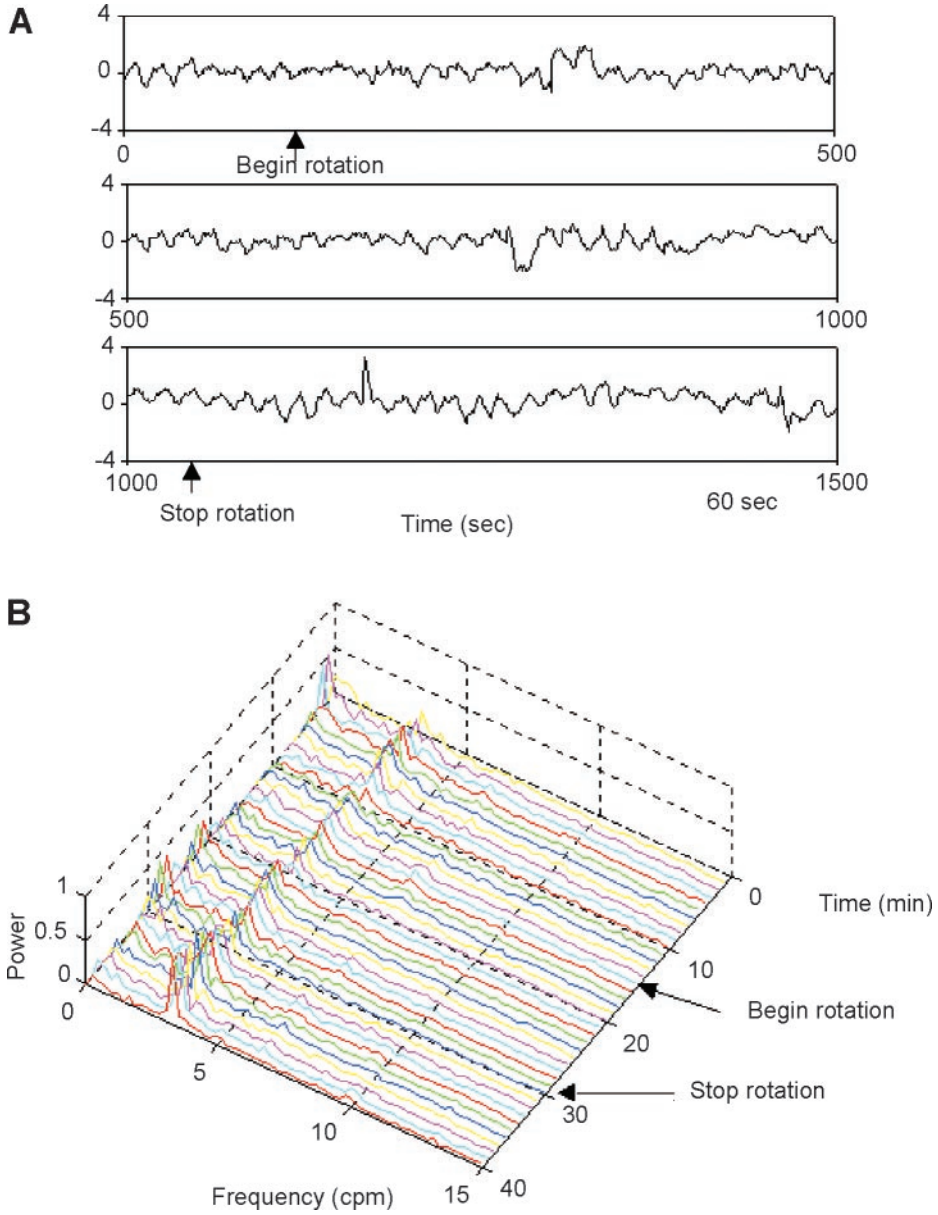


Fig. 3. Raw EGG signals and running spectral analysis of waveform from the subject described in Fig. 2 after pretreatment with ginger (1,000 mg). *A*: the gastric slow wave was 3 cpm at basal and remained relatively stable during vection. *B*: running spectral analysis of the raw EGG signals demonstrated regular oscillation of the slow wave at 3 cpm during circular vection. The subject did not experience nausea.

tively blunted tachygastric activity induced by circular vection, prolonging latency before the onset of tachygastria and shortening its duration after vection stopped.

*Effect of ginger on vection-induced elevation of plasma vasopressin.* The basal plasma vasopressin level was 2.1 ± 0.5 pg/ml. During circular vection, it rose to 5.3 ± 0.4 pg/ml ($P < 0.05$). The administration of ginger at 1,000 and 2,000 mg reduced the vasopressin level to 3.7 ± 0.6 pg/ml ($P < 0.05$) and 2.7 ± 1.2 pg/ml ($P < 0.05$), respectively (Fig. 5). This suggests that ginger may exert its antiarrhythmia and antinausea effects by inhibiting vasopressin release during circular vection.

### *Vasopressin Infusion Studies*

*Effects of ginger on vasopressin-evoked nausea.* Vasopressin infusion at 0.1 and 0.2 U/min iv produced plasma levels of 177.7 ± 108 and 691.7 ± 168.6 pg/ml, respectively. Pretreatment with ginger (2,000 mg) did not affect vasopressin levels (results not shown). During vasopressin infusion, all four subjects reported nausea, the severity of which was rate dependent. At 0.1 U/min, the nausea score was 1.0 ± 0.6, and at 0.2 U/min, the score was 2.3 ± 0.7 ($P < 0.05$, ANOVA), similar to vection-induced nausea scores. Ginger (2,000 mg) had no effect on reducing nausea evoked by either infusion rate (Fig. 6).

*Effects of ginger on vasopressin-evoked gastric dysrhythmias.* Of the four subjects susceptible to motion sickness, three developed prominent bradygastria and one developed mixed bradygastria and tachygastria during the vasopressin infusion. Subjects demonstrated similar dysrhythmic patterns during vasopressin studies with and without ginger, suggesting that ginger pretreatment had little effect on vasopressin-

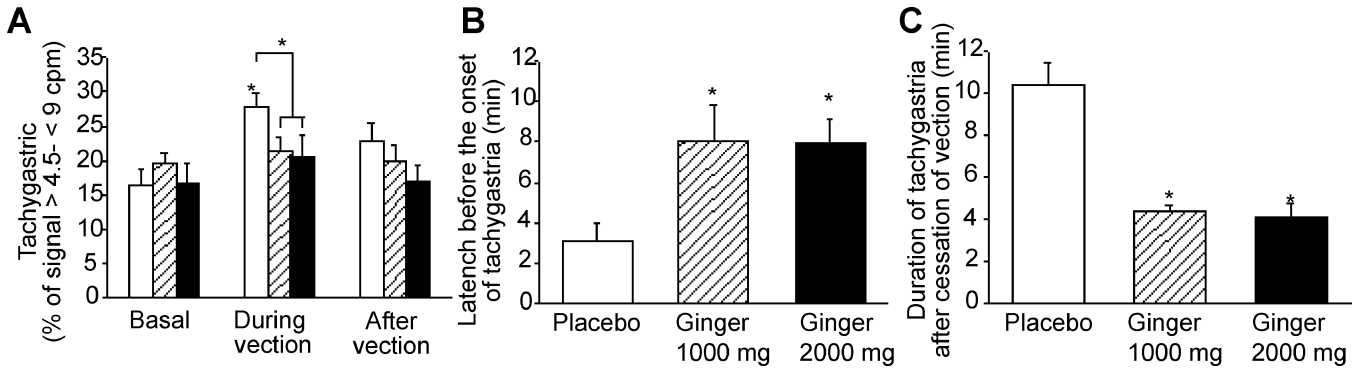


Fig. 4. Tachygastric activity induced by circular vection in subjects pretreated with ginger [1,000 mg (hatched bars), 2,000 mg (filled bars), and in untreated subjects (open bars)]. *A*: a significant increase in activity in the tachygastric frequency range induced by circular vection ($P < 0.05$, compared with basal) was blunted by ginger pretreatment (1,000 and 2,000 mg; $P < 0.05$, compared with control). Ginger pretreatment (1,000 and 2,000 mg) also prolonged latency before tachygastria onset (*B*; $P < 0.05$, compared with control) and reduced the duration of tachygastria after vection cessation (*C*; $P < 0.05$, compared with control). No difference was observed in the effect of 1,000 mg compared with 2,000 mg ginger on the 3 parameters measured. All results are means ± SE ($n = 13$; *$P < 0.05$).

evoked gastric dysrhythmias. Vasopressin infusion induced a rate-dependent increase in the bradygastric activity, 26.8 ± 7.3% at 0.1 U/min and 41.5 ± 9.9% at 0.2 U/min ($P < 0.05$, ANOVA). Ginger pretreatment had no effect on dysrhythmic activity induced by vasopressin infusion (Fig. 7).

## DISCUSSION

The present study showed that ginger at a dose of 1,000 mg effectively reduced the severity of nausea evoked by circular vection, prolonging latency before the onset of nausea and shortening the recovery time from nausea after the cessation of vection. Ginger at a dose of 2,000 mg did not provide further therapeutic effects. Ginger also reduced tachygastria and the elevation in plasma vasopressin induced by circular vection. In other studies performed in our laboratory, ginger had no effect on slow-wave activity under basal conditions and did not cause any symptoms (8). In contrast, ginger did not affect nausea or gastric dysrhythmias evoked by vasopressin infusion. These results suggest that ginger is effective in preventing motion sickness, possibly by suppressing vasopressin release from the central nervous system.

Ginger has been used in China for thousands of years to treat many medical conditions such as dyspepsia, nausea, diarrhea, rheumatism, and toothache (20). In the last 20 years, the effects of ginger in treating

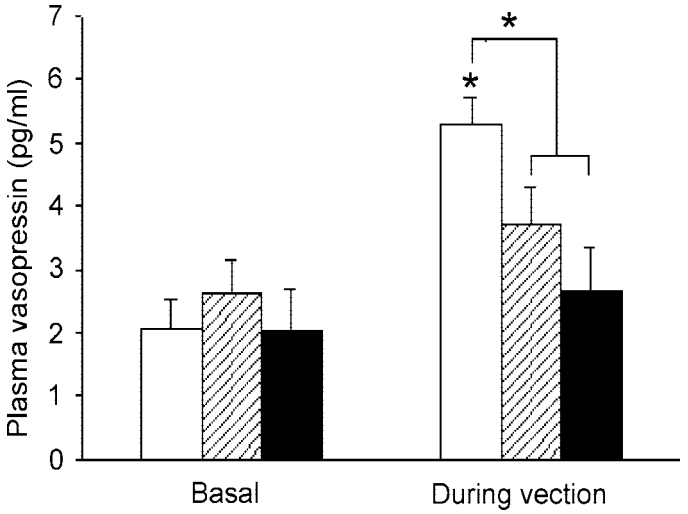


Fig. 5. Effects of ginger pretreatment on plasma vasopressin release induced by circular vection in subjects susceptible to motion sickness. Circular vection induced a significant increase in plasma vasopressin level (*$P < 0.05$, compared with basal). Elevation of plasma vasopressin was reduced by pretreatment with ginger [1,000 mg (hatched bars), 2,000 mg (filled bars); *$P < 0.05$, compared with control (open bars)]. No significant difference was observed between the 2 doses of ginger. All results are means ± SE ($n = 13$).

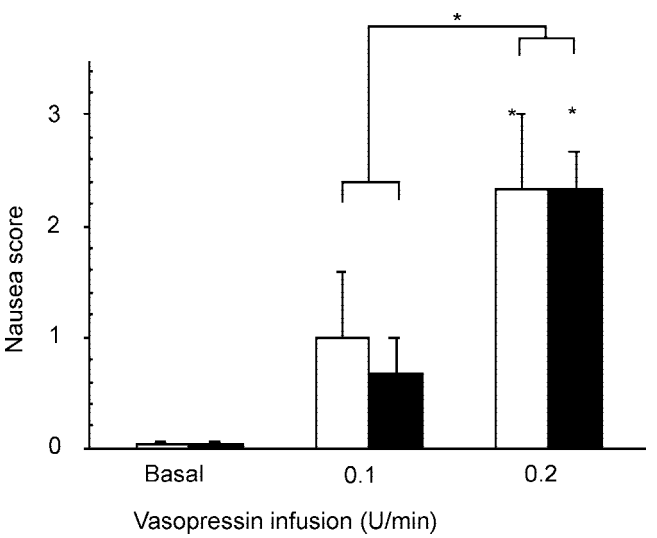


Fig. 6. Effects of vasopressin infusion on nausea with (filled bars) and without (open bars) ginger pretreatment (2,000 mg). Vasopressin infusion induced a dose-dependent effect on nausea, significant at 0.2 U/min (*$P < 0.05$, ANOVA). Note that the severity of nausea was similar to that achieved during circular vection. Ginger pretreatment did not affect nausea induced by vasopressin-infusion (*$P < 0.05$, compared with basal). All results are means ± SE ($n = 4$).

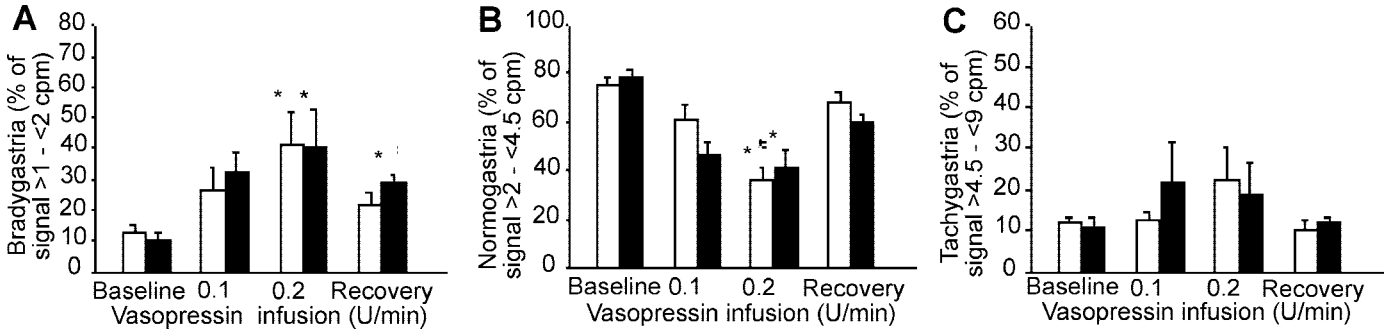


Fig. 7. Effects of vasopressin infusion on the generation of gastric dysrhythmia with (filled bars) and without (open bars) ginger pretreatment (2,000 mg). Vasopressin infusion evoked a dose-dependent increase in the bradygastric frequency range (*A*) and a decrease in activity in the normogastric frequency range (*B*). These changes were significant at an infusion of 0.2 U/min (*$P < 0.05$, ANOVA), although there was no significant change in activity in the tachygastric frequency range (*C*). Ginger pretreatment did not affect the increase in activity in the bradygastric frequency range or the decrease in activity in the normogastric range induced by vasopressin infusion (*$P < 0.05$, compared with basal). All results are means ± SE ($n = 4$).

motion sickness have been reported in three papers; two demonstrated its effectiveness (10, 23) and one did not (28). One of the studies demonstrating ginger's effectiveness was performed at sea and involved 80 naval cadets unaccustomed to sailing; ginger reduced the tendency to vomit and the incidence of cold sweats compared with placebo (10). Ginger has also been found to effectively reduce rotation-induced nausea. Mowrey and Clayson (23) used a rotating chair to induce nausea and vomiting in 36 undergraduates with a history of motion sickness. Ginger offered better protection against nausea induced by circular vection, compared with dimenhydrinate and placebo (23). In contrast, Stewart and colleagues (28) conducted a placebo-controlled study and reported that none of the ginger preparations provided protection against motion sickness, compared with placebo. The dissimilarity of results reported by Stewart and colleagues (28) compared with those of Mowrey and Clayson (23) and of our investigation may be related to methods of symptom reporting. In our study, subjects were asked to report only nausea and its severity during vection, and most of our subjects experienced severe nausea or vomiting. Similarly, Mowrey and Clayson used perceived stomach feeling as the only subjective scoring symptom. Stewart and colleagues developed the M-III score for symptom reporting; a system based on a combination of five cardinal symptoms of motion sickness: nausea, pallor, cold sweats, increased salivation, and drowsiness (9). It is not known whether ginger reduced symptoms other than nausea. Our study showed that in addition to lowering maximal nausea scores, ginger also prolonged latency before the first perception of nausea and shortened the duration of nausea after vection cessation, further supporting the protective effect of ginger against nausea associated with motion sickness.

Another factor that may affect study outcome relates to the subjects' susceptibility to motion sickness (22). We recruited subjects based on prior histories of motion sickness and qualified them by exposure to circular vection before enrollment. This method of subject selection was similar to that of Mowrey and Clayson, whereas Stewart and associates randomly selected subjects from a pool of healthy individuals. The inclusion of individuals resistant to motion sickness may affect study results.

The mechanism by which ginger prevents motion sickness is poorly understood. It has been postulated that ginger ameliorates the effects of motion sickness through its aromatic, carminative, and possible absorbent properties, which are thought to block gastrointestinal reactions and subsequent nausea feedback (23). Unlike most central acting antimotion sickness drugs, ginger was not able to reduce vestibular and optokinetic nystagmus (21). This suggests that ginger may exert its action peripherally and explains the lack of central side effects, such as drowsiness, common to all centrally acting antiemetics. This does not, however, conclusively exclude the possibility that ginger may act centrally. The pharmacologically active components of ginger are relatively small molecules that should be capable of crossing the blood-brain barrier. In fact, a major component of ginger, [6]-gingerol, was shown to prevent vomiting in response to cyclophosphamide in an animal study (16).

Motion sickness experimentally induced by circular vection was recently found to be associated with gastric dysrhythmias (27). Gastric dysrhythmias appear to be pathogenically important, because they reliably developed within 1–2 min before the induction of nausea, and the extent of disruption of the gastric pacemaker activity was correlated positively with the severity of nausea (11, 27, 33). In the present study, we demonstrated that a 1,000-mg oral dose of ginger simultaneously reduced the severity of nausea and the degree of gastric dysrhythmias evoked by circular vection, supporting the possibility that ginger exerts its antinausea effect by preventing the development of gastric dysrhythmias. Increasing the dose to 2,000 mg did not produce additional benefits for gastric dysrhythmias nor for the development of nausea, suggesting that the maximal efficacy of ginger had been reached with the 1,000-mg dose.

The mechanisms responsible for the generation of gastric dysrhythmias with motion sickness are incompletely understood. The ability of muscarinic receptor antagonists such as atropine and scopalamine to prevent both nausea and gastric slow-wave disruption induced by circular vection suggests an important role for the cholinergic neural pathway (11, 31). Ginger has been proposed to possess anticholinergic effects at both central and peripheral sites (24). Hence, the possibility that ginger exerts its antiemetic effects by acting on cholinergic-dependent pathways deserves further investigation. Ginger has also been shown to be a potent inhibitor of prostaglandin and leukotriene synthesis and has demonstrated anti-5-$HT_3$ effects (13, 34). Blockage of the 5-$HT_3$ pathway has been shown to reduce nausea and vomiting in several clinical conditions (2, 29). In addition, research has demonstrated that gastric slow-wave rhythm disturbances in response to certain physiological stimuli are mediated by endogenous prostaglandin production (12, 15, 19). However, it is unlikely that ginger exerts its antimotion sickness effects via these pathways, because, as we have previously demonstrated, gastric dysrhythmias associated with motion sickness are mediated by prostaglandin- and 5-$HT_3$-independent pathways (2, 11, 29).

Investigations have demonstrated elevations in plasma vasopressin concurrent with disruption of slow-wave rhythmicity during circular vection-induced motion sickness. This raises the possibility that release of vasopressin into the peripheral circulation might play a pathogenic role in both the induction of symptoms and generation of gastric dysrhythmias (18, 33). It is known that some patients who receive vasopressin develop nausea (30). On the other hand, we have demonstrated that in contrast to an infusion of a supraphysiological dose of vasopressin, vasopressin infusion in humans to a plasma level similar to that evoked by circular vection does not induce nausea or gastric dysrhythmias (14). We have postulated that cofactors in addition to vasopressin release may be needed for full induction of the symptomatic and slow-wave disruptions with motion sickness (14). Also, as central neural, rather than peripheral neural, muscarinic antagonists are prophylactic against induction of motion sickness and as vasopressin is released by the posterior pituitary into a local portal circulation, it is likely that central, rather than peripheral, actions of vasopressin are responsible for the observations of this and our prior investigation. In the present study, doses of ginger that effectively reduced vection-induced nausea and dysrhythmias also reduced vection-induced vasopressin release; these same doses, however, were ineffective in preventing nausea or gastric dysrhythmias induced by exogenous vasopressin infusion. Therefore, ginger may prevent the release but not the action of vasopressin in the induction of gastric dysrhythmias and nausea.

In conclusion, we have demonstrated that ginger effectively reduces nausea, tachygastric activity, and the release of vasopressin induced by circular vection. In this manner, ginger may act as a novel agent in the prevention and treatment of motion sickness.

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