Gastrointestinal motor and myoelectric correlates of motion sickness

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Lang, Ivan M., S. K. Sarna, and R. Shaker. Gastrointestinal motor and myoelectric correlates of motion sickness. Am. J. Physiol. 277 (Gastrointest. Liver Physiol. 40): G642–G652, 1999.—The objectives of this study were to characterize the digestive tract motor and myoelectric responses associated with motion sickness. Twenty-two cats (1.5–3.0 kg) were chronically implanted with force transducers and electrodes on the stomach and small intestine. Motion sickness was activated by vertical oscillation (VO) at ±0.5 g and identified as salivation, licking, or vomiting. Vomiting was initiated chemically by UK-14304 (2.5–15 µg/kg iv) or CuSO₄ (10–50 mg ig). We found that VO caused vomiting (45% of trials), a decrease in gastrointestinal (GI) motility (69% of trials), salivation or licking (59% of trials), bradygastria (39% of trials), retrograde giant contraction (RGC, 43% of trials), giant migrating contraction (GMC, 5% of trials), and defecation (18% of trials). The decrease in GI motility occurred with (62% of trials) or without (69% of trials) vomiting. Motion sickness was accompanied by bradygastria (52% of trials) and decreased GI motility (70% of trials). Similar events occurred after CuSO₄ and UK-14304, but the incidences of responses after CuSO₄ were less frequent, except for vomiting, RGC, and GMC. UK-14304 never caused GMCs or defecation. The magnitude and velocity of the RGC were the same during all emetic stimuli, and RGCs never occurred without subsequent vomiting. Supradiaphragmatic vagotomy (n = 1) or atropine (n = 2, 10 or 50 µg/kg iv) blocked the RGC, but not vomiting, due to VO. We concluded that 1) oculovestibular stimulation causes digestive tract responses similar to other types of emetic stimuli, 2) decreased GI motility and bradygastria may be physiological correlates of the motion sickness, and 3) motion sickness may not be dependent on any specific GI motor or myoelectric response.

vomiting; digestive tract motility; myoelectric activity; electrical control activity; gastric dysrhythmia; vagotomy

MOTION SICKNESS has been studied for well over 100 years (21), and to a large extent it remains as much a mystery today as ever. Tyler and Bard (59) defined it as “a specific disorder which is evoked in susceptible persons and animals when they are subjected to movements which have certain characteristics.” Chinn and Smith (10) listed the symptoms of motion sickness to include anorexia, drowsiness, pallor, epigastric awareness, malaise, cold sweat, nausea, vomiting, retching, salivation, headache, increased intestinal peristalsis, fatigue, and mental depression. Animals exhibit many of the same physiological correlates of motion sickness as humans, including salivation, sweating, drowsiness, vomiting, and bowel urgency or defecation (5, 6, 33, 55). It is unknown whether animals exhibit specific digestive tract motor responses associated with motion sickness and whether the digestive tract correlates of motion sickness in animals are similar to those in humans. Investigation of this issue in animals may provide a basis for understanding the role of the digestive tract during motion sickness in humans.

Many early investigators theorized that the gastrointestinal (GI) tract was a source of receptors that initiated some of the symptoms of motion sickness because of the feeling of epigastric awareness (19). Many investigators have correlated changes in digestive tract motor (i.e., decreased lower esophageal sphincter tone) with motion sickness, but a cause-and-effect relationship has not been established.

The motor and myoelectric responses of the GI tract during oculovestibular system-induced (e.g., motion-,vection-, space-, caloric vestibular stimulation-induced) sickness are unclear, because it is difficult to measure these variables in humans, and these events have not been investigated in animals. Here, we refer to all forms of oculovestibular system-induced sickness as motion sickness, although it should be recognized that responses activated during different stimuli may not be identical (5). Direct evidence in humans indicates that motion sickness is associated with decreased lower esophageal sphincter tone (9), decreased gastric tone and motility (12, 35, 64), and initiation or alteration of the migrating motor complex (1, 27, 57). Other indirect evidence suggests that GI motor activity may be suppressed, because motion sickness has been associated with decreased gastric emptying (42, 52, 57, 65), decreased intestinal borborygmy (58), and increased oro-cecal transit time (38). Although the gastric motor effects of motion sickness have been identified in humans (12, 35, 38, 42, 52, 57, 64, 65) and dogs (4), the intestinal motor effects of motion sickness have not been characterized in any species.

The retrograde giant contraction (RGC) is one of the most prominent of the digestive tract motor responses associated with vomiting initiated by chemical stimuli (2, 3, 14, 30, 50, 63), but it is unknown whether the RGC occurs during motion sickness. Studies in humans have suggested the presence of a contraction that causes gastric reflex associated with nausea or motion sickness (1, 33), but an RGC was not recorded. These studies are the first to investigate whether the RGC or...
other specific GI motor correlates of vomiting are associated with motion sickness.

The aims of this study were 1) to characterize and quantify the GI motor and myoelectric correlates of motion sickness, 2) to determine whether the GI correlates of motion sickness differ from those found in other forms of vomiting [i.e., stimulation of the chemoreceptor trigger zone (CTZ) or GI afferents], 3) to determine whether the GI correlates of vomiting as identified in the dog also occur in the cat, and 4) to determine in part the neuropharmacological mechanisms of the digestive tract responses to motion sickness.

**METHODS**

**Animal Selection and Preparation**

Twenty-two cats of either gender weighing 1.5–3.0 kg were preselected for their susceptibility to motion sickness, i.e., vomiting within 10 min of vertical oscillation. The cats were anesthetized with Biotal (25 mg/kg iv) and, with use of aseptic techniques, were surgically implanted with strain gauge force transducers on the digestive tract at the following distances from the pylorus: antrum, 2 cm (A); duodenum, 5 cm (D); jejunum, 25–40 cm (J1); jejunum, 50–90 cm (J2); ileum, 100–150 cm (I). The transducers were oriented to record circular muscle contractile activity. Bipolar silver wire electrodes were sewn onto the gastric antrum (1 cm from the pylorus) to record myoelectric activity. The wires from the recording devices were connected to an Amphenol plug (19 pin) embedded in a dental acrylic cannula, which was sewn across the abdominal wall. This cannula allowed attachment of the strain gauges and electrodes to external amplifiers via a cable. A polyethylene catheter (medical grade Tygon tubing) was implanted in the gastric fundus, and a silicone rubber catheter was implanted into the jugular vein. The opposite end of each catheter was fitted with an intravenous catheter plug and implanted subcutaneously in the back of the neck. Gastric and venous catheters allowed nontraumatic but accurate measurement of all instruments. After the animals were connected to the recording equipment, measurements were obtained for a control period of 10–15 min. This control period was followed by expirations of all instruments. After the animals were connected to the recording equipment, measurements were obtained for a control period of 10–15 min. This control period was followed by 10 min of vertical oscillation through a Grass model 7D polygraph and Vetter tape recorder. The signals from the strain gauges and electrodes were fed into a Grass model 7D polygraph and Vetter tape recorder. The following variables were quantified from the polygraph recordings: electrical control activity (ECA) disruption, RGC magnitude and duration at different levels of the GI tract, and RGC velocity. At a later date the tapes were played back through CODAS (Dataq Instruments, Akron, OH) data acquisition hardware and software and stored.

**Activation of Motion Sickness by Chemical Stimuli**

The responses to vertical oscillation were compared with vomiting activated by chemical stimulation of emetic receptors. Digestive tract receptors were activated by the intragastric injection of CuSO4 (61) at a dose of 10–50 mg dissolved in 2–3 ml of water. The CTZ was stimulated (29) by the intravenous administration of UK-14304 [an α2-adrenoreceptor agonist (8)] at a dose of 2.5–15 µg/kg in a total volume of 0.1 ml given in a rapid bolus injection. The delay to vomiting was ~2 min for intravenous administration of emetics and 2–40 min for intragastric administration of emetics. The cats were not stimulated by chemical stimulation more than once in 2 wk to prevent habituation (13).

**Effects of Vagotomy**

In three cats the effects of supradiaphragmatic vagotomy on the digestive tract responses associated with motion sickness were examined. After control responses were recorded, the cats were prepared for sterile surgery as described above. During surgery the chest was opened between the eighth and ninth ribs, the vagus nerves (dorsal and ventral) just above the diaphragm were transected, and a 1-cm section of each was removed.

**Effects of Cholinergic Antagonist**

The effects of atropine methyl nitrate, a cholinergic antagonist that does not readily cross the blood-brain barrier (20, 30), on the responses to vertical oscillation were examined in two animals. Atropine was given at 10–50 µg/kg iv.

**Data Acquisition and Playback**

The signals from the strain gauges and electrodes were fed into a Grass model 7D polygraph and Vetter tape recorder. The following variables were quantified from the polygraph recordings: electrical control activity (ECA) disruption, RGC magnitude and duration at different levels of the GI tract, and RGC velocity. At a later date the tapes were played back through CODAS (Dataq Instruments, Akron, OH) data acquisition hardware and software and stored.

**Quantification of Data**

Incidence and timing of events. The incidence of events was calculated as the number of successes divided by the number of trials for all animals investigated. The delay to an event was measured from the time of the beginning of the stimulus
Table 1. Incidence of digestive tract responses to emetic stimuli

<table>
<thead>
<tr>
<th>Response</th>
<th>Vertical Oscillation</th>
<th>CuSO₄</th>
<th>UK-14304</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>25/56 = 45% (22)</td>
<td>17/37 = 46% (14)</td>
<td>32/38 = 84% (16)</td>
</tr>
<tr>
<td>RGC</td>
<td>24/56 = 43% (22)</td>
<td>17/37 = 46% (14)</td>
<td>30/38 = 79% (16)</td>
</tr>
<tr>
<td>GMC</td>
<td>3/56 = 5% (22)</td>
<td>9/37 = 24% (14)</td>
<td>0/38 = 0% (16)</td>
</tr>
<tr>
<td>Decrease GI motility</td>
<td>34/49 = 69% (21)</td>
<td>1/34 = 3% (13)</td>
<td>NA†</td>
</tr>
<tr>
<td>Bradygastria</td>
<td>16/41 = 39% (19)</td>
<td>3/26 = 12% (11)</td>
<td>1/24 = 4% (11)</td>
</tr>
<tr>
<td>Salivation</td>
<td>10/56 = 18% (22)</td>
<td>1/37 = 3% (14)</td>
<td>0/38 = 0% (16)</td>
</tr>
<tr>
<td>Licking</td>
<td>19/56 = 34% (22)</td>
<td>3/37 = 8% (14)</td>
<td>8/38 = 21% (16)</td>
</tr>
<tr>
<td>Salivation or licking</td>
<td>26/56 = 46% (22)</td>
<td>3/37 = 8% (14)</td>
<td>23/38 = 61% (16)</td>
</tr>
<tr>
<td>Bradygastria/vomiting</td>
<td>33/56 = 59% (22)</td>
<td>6/37 = 16% (14)</td>
<td>29/38 = 76% (16)</td>
</tr>
<tr>
<td>Bradygastria/no vomiting</td>
<td>8/24 = 33% (6)</td>
<td>3/12 = 25% (8)</td>
<td>7/18 = 39% (11)</td>
</tr>
<tr>
<td>Decrease GI motility/vomiting</td>
<td>8/12 = 25% (9)</td>
<td>0/14 = 0% (8)</td>
<td>4/7 = 57% (4)</td>
</tr>
<tr>
<td>Bradygastria/salivation, licking, vomiting</td>
<td>13/21 = 62% (10)</td>
<td>NA§</td>
<td>NA§</td>
</tr>
<tr>
<td>Bradygastria/salivation, licking, vomiting</td>
<td>14/19 = 69% (16)</td>
<td>NA§</td>
<td>NA§</td>
</tr>
<tr>
<td>Decrease GI motility/no vomiting</td>
<td>13/25 = 52% (13)</td>
<td>NA§</td>
<td>8/19 = 42% (13)</td>
</tr>
<tr>
<td>Decrease GI motility/salivation, licking, vomiting</td>
<td>21/30 = 70% (13)</td>
<td>NA§</td>
<td>NA§</td>
</tr>
</tbody>
</table>

Values are successes/attempt; numbers in parentheses represent number of animals. RGC, retrograde giant contraction; GMC, giant migrating contraction; GI, gastrointestinal; NA, not applicable. *P < 0.05; †P < 0.01 vs. vertical oscillation (by χ² test). §Delay (–90 s) between stimulus and response was too short to evaluate effects of agent on spontaneous motility. ¶Incidence of this event was too low for meaningful statistics.

to the time of the beginning of the response or the last occurrence of the ongoing activity (e.g., for the decrease in GI motility). The duration of an event was measured from the last occurrence of ongoing activity to its first reappearance. For events that occurred at multiple sites (e.g., the RGC or the decrease in GI motility), the time of occurrence at the first site was considered the start of the response and the time of cessation at the first site was considered the end of the response.

The electrical activity of the gastric antrum and small intestine consists of electrical control activity (ECA), also called slow waves or basic electrical rhythm, and electrical response activity (ERA), also called spike activity (44). The ECA is a myogenic event representing the omnipresent oscillation of membrane potential of GI smooth muscle, which is not directly related to functionally important contractions but controls the excitability of the muscle to contract. The ECA, recorded extracellularly, occurs as a single uniform electrical waveform of usually stable frequency and amplitude. The ERA is electrical activity of the smooth muscle that is activated by neurochemical stimuli. The ERA occurs as single or multiple spike potentials, and the number and frequency of response potentials are directly related to the strength and duration of contractions. Bradygastria was defined previously as a decrease in gastric ECA frequency (44, 66) and identified in these studies as an increase in ECA with a 5% amplitude rise (11, 45). Bradygastria was activated by neurochemical stimuli. The ERA occurs as an electrical activity of the smooth muscle that is not directly related to functionally important contractions but controls the excitability of the muscle to contract. The ECA, recorded extracellularly, occurs as a single uniform electrical waveform of usually stable frequency and amplitude. The ERA is electrical activity of the smooth muscle that is activated by neurochemical stimuli. The ERA occurs as single or multiple spike potentials, and the number and frequency of response potentials are directly related to the strength and duration of contractions.

We found that vertical oscillation was successful in activating motion sickness, i.e., licking, salivation, or vomiting, as well as a number of digestive tract responses, including the decrease in GI motility and the decrease in gastric ECA frequency. In contrast to humans and dogs, in cats, giant migrating contractions (GMCs) occur randomly at all levels of the small intestine. These GMCs occur about once every 2–5 h, and each GMC propagates ~40 cm (46).

Table 2. Timing characteristics of the digestive tract responses to emetic stimuli

<table>
<thead>
<tr>
<th>Response</th>
<th>Vertical Oscillation</th>
<th>CuSO₄</th>
<th>UK-14304</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delay to vomit</td>
<td>7.2 ± 1.3 (9)</td>
<td>21.5 ± 5.4 (9)</td>
<td>2.4 ± 0.3 (10)</td>
</tr>
<tr>
<td>Delay to decrease in GI motility</td>
<td>1.6 ± 0.3 (17)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Delay to bradygastria</td>
<td>2.2 ± 0.4 (13)</td>
<td>NA</td>
<td>0.5 ± 0.1 (3)</td>
</tr>
<tr>
<td>Duration of bradygastria</td>
<td>5.2 ± 0.6 (13)</td>
<td>NA</td>
<td>3.9 ± 1.5 (3)</td>
</tr>
<tr>
<td>Delay to salivation</td>
<td>4.3 ± 0.6 (8)</td>
<td>NA</td>
<td>1.4 ± 0.6 (5)</td>
</tr>
<tr>
<td>Duration of salivation</td>
<td>4.6 ± 1.0 (8)</td>
<td>NA</td>
<td>1.4 ± 0.3 (5)</td>
</tr>
<tr>
<td>Delay to RGC</td>
<td>6.6 ± 1.3 (9)</td>
<td>20.7 ± 5.4 (9)</td>
<td>1.7 ± 0.3 (11)</td>
</tr>
</tbody>
</table>

Values are means ± SE in minutes; numbers in parentheses represent number of animals. NA, not applicable because of insufficient number of animals (< 3); see Table 1 footnote for definition of other abbreviations.
creased spontaneous motor activity of the GI tract, bradygastria, RGC, GMC, and defecation. Vomiting induced by vertical oscillation was initiated in 45% of trials, but the other responses occurred at various rates (Table 1). Vomiting was initiated ~7 min after initiation of vertical oscillation, and the other responses occurred in sequence before this time (Table 2).

Salivation or licking. Salivation or licking often (59% incidence) occurred during vertical oscillation, and licking (46% incidence) was more frequent than salivation (34% incidence). These responses occurred ~4 min after the start of vertical oscillation and lasted ~5 min.

Decreased GI motility. Spontaneous GI motility began to decrease ~1.5 min after the initiation of vertical oscillation and continued until the vertical oscillation ended (Table 2, Figs. 1 and 2). The decrease occurred from antrum to jejunum, but only the GI motor activity from antrum to proximal jejunum (J1) decreased significantly (Table 3). This effect was the most frequently (69% incidence) activated response (Table 1) to vertical oscillation, and it occurred equally likely (no significant difference (P > 0.05) by \( \chi^2 \) test) with (62% incidence, Fig. 1) or without vomiting (25% incidence). The bradygastria began ~2 min after vertical oscillation and lasted ~5 min (Table 2). Unlike the decrease in GI motor activity, the bradygastria did not last the duration of the vertical oscillation. Bradygastria was similar [no significant difference (P > 0.05) by \( \chi^2 \) test; Table 1] with (33% incidence) and without vomiting (25% incidence). The bradygastria was not associated with antral contractions (Fig. 1).

RGC and post-RGC phasic contractions. The RGC was activated in 96% of vomiting activated by vertical oscillation and was never activated independent of vomiting (Fig. 1). The RGC began in the middle of the small intestine (70 ± 14 cm from the pylorus) ~6.5 min

This decreased GI motility usually (70% incidence) occurred concomitant with motion sickness (Figs. 1 and 2, Table 1).

Bradygastria. The gastric ECA was often (39% incidence) disrupted because of vertical oscillation, and this response was always characterized as bradygastria (slowing or cessation of ECA) but never tachyarrhythmia or tachyarrhythmia (Fig. 1). The incidence of this bradygastria was similar [no significant difference (P > 0.05) by \( \chi^2 \) test; Table 1] with (33% incidence) and without vomiting (25% incidence). The bradygastria began ~2 min after vertical oscillation and lasted ~5 min (Table 2). Unlike the decrease in GI motor activity, the bradygastria did not last the duration of the vertical oscillation. Bradygastria was similar [no significant difference (P > 0.05) by \( \chi^2 \) test; Table 1] with (33% incidence) and without vomiting (25% incidence). The bradygastria was not associated with antral contractions (Fig. 1).

RGC and post-RGC phasic contractions. The RGC was activated in 96% of vomiting activated by vertical oscillation and was never activated independent of vomiting (Fig. 1). The RGC began in the middle of the small intestine (70 ± 14 cm from the pylorus) ~6.5 min
after initiation of vertical oscillation (Tables 2 and 4, Fig. 1). The magnitude of the RGC differed little in different parts of the GI tract (Table 5), but the duration of the RGC decreased from antrum to ileum (Table 6). Although the average velocity of the RGC from the jejunum was 2.5 ± 0.3 cm/s, the velocity decreased from ileum to antrum (Table 7). A series (3–8) of phasic contractions, the post-RGC phasic contractions, occurred after the RGC at all levels of the GI tract, but the incidence and number of these contractions were highly variable.

GMC. GMCs of the small intestine occurred infrequently (5% incidence) during vertical oscillation (Table 1).

Defecation. Defecation was an occasional (16% incidence) consequence of vertical oscillation.

Small intestinal GMCs never (0 of 10 trials in 6 animals) occurred during defecation.

Comparison of Responses to Vertical Oscillation With CuSO₄-Induced Vomiting

Incidence of responses. Similar to vertical oscillation, CuSO₄-induced RGCs were never observed without vomiting (Table 1, Fig. 3). CuSO₄-induced vomiting was accompanied by more GMCs (Fig. 4) and a lower incidence of bradygastria (Fig. 4), defecation, salivation, and licking than was vertical oscillation. In addition, although the incidence of bradygastria without vomiting was 25% during vertical oscillation, bradygastria without vomiting never occurred after CuSO₄. The incidence of small intestinal GMCs was greater after CuSO₄, similar to vertical oscillation (Table 1). Perhaps the most significant difference between vertical oscillation- and CuSO₄-induced responses was the much lower incidence of decreased GI motility after CuSO₄ (69% vs. 3% incidence, Table 1).

Timing characteristics of responses. The delay to vomiting and RGC was >20 min (Table 2). The number of animals in which the other events occurred was too low to calculate a meaningful average response delay or duration.

RGC characteristics. The intestinal origin, magnitude, duration, or velocity of the RGC due to CuSO₄ did not differ significantly from those activated during vertical oscillation when no drugs were administered (Figs. 3 and 5, Tables 4–7).

Comparison of Responses to Vertical Oscillation With UK-14304-Induced Vomiting

Incidence of responses. Similar to vertical oscillation and CuSO₄-induced responses, the RGC due to UK-14304 never occurred without the subsequent vomiting episode (Fig. 3). Unlike vertical oscillation and CuSO₄, UK-14304 did not activate GMCs or defecation (Table 1). However, the incidence of salivation, licking, and bradygastria activated by UK-14304 was similar to that activated by vertical oscillation (Table 1) and, as with vertical oscillation bradygastria, often (42% incidence) occurred concomitant with salivation or licking (Table 1, Fig. 3).

Timing characteristics of responses. Vomiting and the RGC activated by UK-14304 occurred ~2 min after intravenous administration. Not only was vomiting

Table 3. Effect of vertical oscillation on spontaneous GI motor activity

<table>
<thead>
<tr>
<th>Region of GI Tract</th>
<th>Before VO</th>
<th>During VO</th>
<th>After VO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antrum</td>
<td>52.7 ± 10.9 (7)</td>
<td>24.4 ± 4.4 (7)</td>
<td>38.0 ± 12.6</td>
</tr>
<tr>
<td>Duodenum</td>
<td>45.0 ± 9.5 (9)</td>
<td>29.2 ± 5.9 (9)</td>
<td>36.9 ± 9.8 (9)</td>
</tr>
<tr>
<td>Jejunum (25–40 cm)</td>
<td>39.0 ± 7.6 (9)</td>
<td>28.9 ± 5.1* (9)</td>
<td>31.0 ± 8.2 (9)</td>
</tr>
<tr>
<td>Jejunum (50–90 cm)</td>
<td>40.5 ± 12.0 (9)</td>
<td>30.2 ± 9.3 (9)</td>
<td>31.3 ± 10.8 (9)</td>
</tr>
<tr>
<td>Ileum (100–150 cm)</td>
<td>46.7 ± 11.6 (7)</td>
<td>48.0 ± 12.0 (7)</td>
<td>49.8 ± 20.4 (9)</td>
</tr>
</tbody>
</table>

Values are means ± SE in g/min of integrated motor activity; numbers in parentheses represent number of animals. No significant differences (P < 0.05) were found between group variances by use of Bartlett’s test and between-group means with ANOVA or Tukey’s test.}

Table 5. Magnitude of RGC

<table>
<thead>
<tr>
<th>Region of GI Tract</th>
<th>Vertical Oscillation</th>
<th>CuSO₄</th>
<th>UK-14304</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antrum</td>
<td>90.0 ± 14.5 (8)</td>
<td>60.2 ± 10.7 (6)</td>
<td>66.4 ± 12.0 (8)</td>
</tr>
<tr>
<td>Duodenum</td>
<td>90.0 ± 11.1 (9)</td>
<td>72.8 ± 15.5 (8)</td>
<td>69.0 ± 11.1 (10)</td>
</tr>
<tr>
<td>Jejunum (25–40 cm)</td>
<td>97.2 ± 14.2 (9)</td>
<td>78.8 ± 13.9 (8)</td>
<td>84.2 ± 16.6 (11)</td>
</tr>
<tr>
<td>Jejunum (50–90 cm)</td>
<td>90.4 ± 12.3 (5)</td>
<td>84.0 ± 22.5 (6)</td>
<td>70.4 ± 20.3 (8)</td>
</tr>
<tr>
<td>Ileum (100–150 cm)</td>
<td>84.3 ± 53.4 (3)</td>
<td>62.0 ± 17.5 (5)</td>
<td>71.0 ± 35.6 (4)</td>
</tr>
</tbody>
</table>

Values are means ± SE in grams of force; numbers in parentheses represent number of animals. No significant differences (P < 0.05) were found between group variances by use of Bartlett’s test and between-group means with ANOVA or Tukey’s test.

Table 4. Miscellaneous variables and responses to emetic stimuli

<table>
<thead>
<tr>
<th>Variable</th>
<th>CuSO₄</th>
<th>UK-14304</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical Oscillation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RGC origin, cm</td>
<td>70 ± 14 (9)</td>
<td>87 ± 12 (9)</td>
</tr>
<tr>
<td>Total SI length, cm</td>
<td>138 ± 5 (9)</td>
<td>132 ± 6 (9)</td>
</tr>
<tr>
<td>RGC origin, % SI</td>
<td>50 ± 9 (9)</td>
<td>65 ± 8 (9)</td>
</tr>
<tr>
<td>Dose</td>
<td>16 ± 2 mg (9)</td>
<td>2.9 ± 0.4 μg/kg (11)</td>
</tr>
</tbody>
</table>

Values are means ± SE; numbers in parentheses represent number of animals. No significant differences (P < 0.05) were found between group variances by use of Bartlett’s test and between-group means with ANOVA or Tukey’s test.

Table 6. Duration of RGC

<table>
<thead>
<tr>
<th>Region of GI Tract</th>
<th>Vertical Oscillation</th>
<th>CuSO₄</th>
<th>UK-14304</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antrum</td>
<td>12.0 ± 0.5 (8)</td>
<td>10.9 ± 0.5 (6)</td>
<td>10.8 ± 0.8 (8)</td>
</tr>
<tr>
<td>Duodenum</td>
<td>8.4 ± 1.0 (9)</td>
<td>8.8 ± 0.7 (8)</td>
<td>8.2 ± 0.6 (10)</td>
</tr>
<tr>
<td>Jejunum (25–40 cm)</td>
<td>7.0 ± 0.7 (9)</td>
<td>7.2 ± 0.7 (8)</td>
<td>6.6 ± 0.5 (11)</td>
</tr>
<tr>
<td>Jejunum (50–90 cm)</td>
<td>5.6 ± 0.6 (5)</td>
<td>6.4 ± 0.8 (6)</td>
<td>5.5 ± 0.7 (8)</td>
</tr>
<tr>
<td>Ileum (100–150 cm)</td>
<td>5.0 ± 1.0 (3)</td>
<td>5.0 ± 0.5 (5)</td>
<td>4.8 ± 0.7 (4)</td>
</tr>
</tbody>
</table>

Values are means ± SE in seconds; numbers in parentheses represent number of animals. No significant differences (P < 0.05) were found between group variances by use of Bartlett’s test and between-group means with ANOVA or Tukey’s test.
initiated sooner than after vertical oscillation, other responses, i.e., bradygastria and salivation, occurred sooner as well (Table 2, Fig. 3).

**RGC characteristics.** The origin in the small intestine, magnitude, duration, and velocity of the RGC activated by UK-14304 were not significantly different from those of RGC activated by vertical oscillation or CuSO₄ (Tables 4–7, Figs. 3 and 5).

**Effects of Supradiaphragmatic Vagotomy**

We found that after supradiaphragmatic vagotomy the RGC (0 of 3 animals) did not occur, but the decrease in GI motility (2 of 3), bradygastria (2 of 2), salivation (3 of 3), vomiting (1 of 3), GMCs (1 of 3), or defecation (1 of 3) did occur (Fig. 6). Because of dysfunction of strain gauges or electrodes, full results from all three animals were not obtained.

**Effects of Atropine Methyl Nitrate**

We found that after atropine methyl nitrate administration the RGC (0 of 2 animals), salivation (0 of 2), GMC (0 of 2), and defecation (0 of 2) did not occur, but vomiting (2 of 2), bradygastria (1 of 2), licking (2 of 2), and the post-RGC phasic contractions (1 of 2) did occur (Fig. 7). Atropine inhibited ongoing GI motor activity; therefore, its specific effect on the decreased GI motor activity caused by vertical oscillation was indeterminate.

**DISCUSSION**

These studies are the first to characterize and quantify the GI motor responses during motion sickness and to relate these events with changes in gastric myoelectric activity and other digestive tract responses. We found that vertical oscillation activated motion sickness in cats and that these cats exhibited similar GI motor responses, i.e., the RGC and post-RGC phasic contractions, as have been identified previously in dogs during chemically induced vomiting (28, 30). Although the magnitude, duration, and velocity of the RGC were different in cats, the RGC occurred in similar portions of the digestive tract and had a similar relationship with vomiting. One significant difference was that in dogs the GI motor correlates of vomiting could be readily activated without activating retching and vomiting (30), but this never occurred in the cat. The functional significance of this difference is unknown.

Vomiting can be initiated from various receptors located in the periphery as well as the brain. These include the oculovestibular system for motion sickness.

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**Table 7. Velocity of the RGC**

<table>
<thead>
<tr>
<th></th>
<th>Vertical Oscillation</th>
<th>CuSO₄</th>
<th>UK-14304</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenum to antrum</td>
<td>0.8 ± 0.1 (8)</td>
<td>0.7 ± 0.1 (6)</td>
<td>0.6 ± 0.1 (7)</td>
</tr>
<tr>
<td>J. jejunum (40 cm)</td>
<td>3.3 ± 0.3 (9)</td>
<td>2.9 ± 0.3 (9)</td>
<td>2.9 ± 0.2 (10)</td>
</tr>
<tr>
<td>J. jejunum (90 cm)</td>
<td>4.7 ± 1.2 (5)</td>
<td>6.0 ± 1.2 (7)</td>
<td>4.6 ± 1.4 (9)</td>
</tr>
<tr>
<td>I. ileum (150 cm)</td>
<td>6.8 ± 2.1 (3)</td>
<td>6.5 ± 1.8 (5)</td>
<td>6.2 ± 3.0 (4)</td>
</tr>
<tr>
<td>J. jejunum (90 cm)</td>
<td>2.5 ± 0.3 (5)</td>
<td>2.8 ± 0.3 (4)</td>
<td>2.2 ± 0.4 (6)</td>
</tr>
</tbody>
</table>

Values are means ± SE in cm/s; numbers in parentheses represent number of animals. No significant differences (P < 0.05) were found between group variances by use of Bartlett's test and between-group means with ANOVA or Tukey's test.
(37, 62), the digestive tract for emesis due to ingestion of noxious substances (61), and the CTZ for emesis due to circulating agents (7). On the basis of studies in dogs in which digestive tract responses to emetic agent activation of the CTZ (i.e., apomorphine, intravenously) and digestive tract (i.e., CuSO₄, intragastrically) were compared, we previously concluded that although the receptive pathways may be different, all sensory pathways converge on a common preprogrammed motor output (28, 30) to the digestive tract. The fact that the RGC activated during motion sickness was not significantly different from that activated by CuSO₄ or UK-14304 further corroborates our prior conclusion.

In a prior study in the dog (30), we investigated the neuropharmacological mechanisms of the RGC and post-RGC phasic contractions and found that these events were mediated by the vagus nerves. Although only one animal was tested, this conclusion was confirmed in our present studies using the cat, because supradiaphragmatic vagotomy eliminated the digestive tract responses associated with vomiting. In addition, in the dog we (30) found that the RGC was mediated by muscarinic cholinergic receptors. This finding was also confirmed in the present studies using cats (n = 2), inasmuch as the RGC, but not the post-RGC, phasic contractions were blocked by atropine. Furthermore, it is unlikely that these GI motor correlates of vomiting are mediated by the sympathetic nervous system, because sympathetic splanchnic nerve denervation did not block these events in the dog (30).

Vertical oscillation not only activated vomiting and its GI motor correlates but also caused a general decrease in GI motility. This decreased GI motility was not observed after administration of the other emetic stimuli and occurred equally likely whether vomiting occurred or not, suggesting that this response was

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**Fig. 4.** Activation of giant migrating contraction (GMC) and RGC by CuSO₄. See Fig. 1 legend for definition of abbreviations.

**Fig. 5.** Comparison of RGCs activated by vertical oscillation, CuSO₄, and UK-14304. See Fig. 1 legend for definition of abbreviations. Note similarity of RGCs activated by different stimuli.
related to the unusual motion rather than to vomiting or the other emetic sensory pathways (i.e., CTZ or GI tract). This decreased GI motility may be a motor correlate of motion sickness, because it usually (in 70% of trials) occurred concomitant with the indexes of motion sickness (i.e., salivation, licking, or vomiting). This generalized decrease in upper GI motility during oculovestibular stimulation may at least partly explain the decreased borborygmy (58), increased orocecal transit time (38), and decreased gastric emptying (42, 52, 57, 65) observed in humans during motion sickness. This decreased GI motility occurred more frequently and earlier than the other indexes of motion sickness, which suggests that this GI motor response may be a more sensitive autonomic index of motion sickness. Perhaps salivation and licking are delayed relative to the GI response because of the temporal delay between neural stimulation of salivation and the visible oral response. The decrease in GI motor activity was not blocked by vagotomy (n = 2); therefore, it is probably mediated by the splanchnic rather than the vagus nerves.

A significant and early response to motion sickness in cats, as in humans, is a disruption of gastric myoelectric activity (17, 48, 51). In contrast to humans, who have most often been characterized as having a rapid electrogastrogram (EGG) rate (i.e., tachygastria (17, 48, 49) or tachyarrhythmia (26, 60)) during motion sickness, the cats exhibited bradygastria only. There are two significant differences in techniques, however, between our studies and most of the human studies. We recorded gastric ECA directly from the gastric seromuscular layer, and in human studies EGG was recorded from the skin overlying the stomach (17, 48, 51). Also, we counted ECA directly, because the ECA waves were clear and readily identifiable in the animal studies, whereas human recordings of EGG required computer-based spectral analysis (17, 48, 51). We do not know whether the differences in gastric myoelectric responses observed in humans and cats are due to technical or species differences. Technical differences may be significant, because it has been found that EGG recordings poorly identify ECA uncoupling or orad spread, which can be misinterpreted as tachygastria, tachyarrhythmia, or bradygastria (15, 33, 36).

Differences in responses between the cat and human studies may also be attributed to differences in sensory mechanisms. Motion sickness was activated by vection, i.e., illusory self-motion caused by a rotating drum, in the human studies (17, 18, 26, 38, 48, 49, 51); we used vertical oscillation in these cat studies. It is unlikely that differences in stimuli were responsible for this difference in response, because similar responses (i.e., dysrhythmias) have been found with different stimuli in human and animal studies. Similar dysrhythmias (tachygastria or tachyarrhythmia) have been found with use of the similar EGG recording techniques in humans experiencing sickness due to vection (17, 26, 38, 48, 49, 51), pregnancy (25), diabetes (22), functional dyspepsia (23), chronic renal failure (34), or hyperthyroidism (40). Similar bradygastrias have been found with use of similar ECA recording techniques in cats and dogs experiencing sickness due to vertical oscillation (this study) or various chemical stimuli (31).

Regardless of the specific effect on gastric myoelectric activity, cats as well as humans exhibit an alteration in gastric myoelectric activity that precedes vomiting due to motion sickness. This change in myoelectric activity occurred whether the cats vomited or not and was observed in 52% of trials in which motion sickness (i.e., salivation, licking, or vomiting) occurred. Therefore bradygastria, like the decrease in GI motility, may also be an autonomic physiological correlate of motion sickness, although it is less reliable. The onset of bradygastria was also more rapid than salivation, similar to the
decrease in GI motility. Therefore, bradygastria may be an index of motion sickness in cats, as tachygastria is an index of motion sickness in humans. In addition, similar (56, 66) to tachygastria and tachyarrhythmia in humans, no gastric antral contractions occurred concomitant with bradygastria in the cats. This bradygastria was probably not mediated by the vagus nerves or muscarinic cholinergic receptors, because vagotomy (n = 2) or atropine (n = 2) did not block bradygastria but did block other responses associated with motion sickness. Similarly, it has been found that the vagus nerves (53) or peripheral muscarinic cholinergic receptors (18) do not mediate the gastric dysrhythmias of humans.

Our findings suggest that gastric ECA disruption, decreased GI motility, RGC, and post-RGC phasic contractions are physiological correlates of motion sickness, but motion sickness is not dependent on any of these responses. Motion sickness sometimes occurred without these responses, and elimination of some of these responses by vagotomy or atropine did not block motion sickness. Therefore, we concluded that these GI events are part of a constellation of autonomic responses, including salivation, licking, drowsiness, sweating, and pallor, that form a set of precursors to oculovestibular stimulation-induced vomiting referred to in animals as the prodromata (37). Not all responses occur in all individuals at all times, perhaps because the final combination of autonomic responses depends on the psychological state of the individual and the ongoing state of the autonomic nervous system.

One of the main symptoms of motion sickness in humans is the feeling of nausea (10). Nausea cannot be quantified or conclusively identified in animals, because it is a feeling. However, animal studies can be useful in the study of nausea if the physiological correlates of the sensation can be identified from human studies. That is, just as animals can be used as models for humans of systems we cannot easily measure, e.g., GI motility, then humans can be used as models for animals of systems we cannot easily measure, e.g., sensation. Therefore, animals are often used in pain studies (47), even though the pain cannot be measured directly. In the case of pain, human studies have shown that pain is associated with changes in heart rate, blood pressure, and respiratory rate (16). Therefore, if one applies a stimulus, noxious to humans, to an animal and its heart rate, blood pressure, and respiratory rates change similar to that of humans and it reacts to the stimulus similar to humans (i.e., attempts to escape the noxious stimulus), we would conclude that the animal felt pain. Similarly, nausea in humans has been associated with various physiological correlates, including disruption of gastric ECA (17, 26, 38, 48, 49, 51, 52, 60). We know from the human experience that if one is subjected to unusual motion to the point of vomiting, this is accompanied by nausea (10, 21, 37, 59). Therefore, in the present studies where we subjected cats to vertical oscillation to the point of motion sickness, the human model predicts that the cats must have felt nausea. During this motion sickness the cats often (50% of the time) exhibited the same physiological response as humans, i.e., gastric ECA disruption. Therefore, although this analysis is speculative and requires further experimentation for confirmation, our results suggest that disruption of gastric ECA may be a physiological correlate of nausea in cats, as it is in humans.

Another digestive tract motor response activated by oculovestibular stimulation is the GMC of the small intestine. This response occurred frequently in response to CuSO$_4$, but not to vertical oscillation or UK-14304. This response is probably due to direct stimulation of the GI tract, inasmuch as these responses are mediated by the enteric nervous system.
In conclusion, we found that motion sickness is associated with GI motor events, e.g., the RGC, similar to those activated by emetic agents in dogs, but unlike dogs these events cannot be activated independent of vomiting. Motion sickness is also accompanied by disruption of gastric myoelectric activity as in humans, but unlike humans we found bradygastria in cats rather than tachygastria or tachyarrhythmia. The most prevalent motor response associated with motion sickness was a decrease in ongoing motor activity of the upper GI tract. The vagus nerves mediate the RGC, but not decreased GI motility or bradygastria associated with motion sickness. Muscarinic cholinergic receptors mediate the RGC but not bradygastria. Motion sickness is not dependent on any of the identified GI motor or myoelectric correlates, including decreased GI motility, bradygastria, RGC, or post-RGC phasic contractions.

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