(1490–2510 ng/dl) the marrow iron score was only 2+ (non-dialysis control value).

In previous studies of serum ferritin and marrow iron,[1-3] no attempt was made to investigate iron overload in the liver and spleen. In the absence of hepatosplenic siderosis the marrow-iron stores can be expected to represent total-body iron stores, and iron-depleted marrow can be regarded as evidence of iron deficiency. This is not true of dialysis haemosiderosis, where there may be a paradox of hepatosplenic iron overload and marrow iron depletion. In this setting, high serum ferritin levels are caused by hepatosplenic siderosis and may not be relied upon as indicators of marrow iron reserves.

All our patients except those in the control group were given relatively large doses of iron dextran, whereas none of the patients in the study of Bell et al.[3] received parenteral iron. Another possible cause of the different results in our study and that of Bell et al.[3] is that the tissue obtained by needle biopsy of bone is usually scanty and crushed and does not allow as accurate an estimate of marrow iron as do large sections of properly prepared bone obtained at necropsy. The solution used to decalcify the bone-marrow sections may cause underestimation of marrow iron, but identical histochemical procedures were used for the dialysis patients' and controls' sections and the results of chemical analyses of tissue iron agreed with the histochemical scores (table).

The fate of hepatosplenic iron stores after intravenous iron-dextran therapy has not been fully investigated. In rabbits the bulk of intravenously injected iron dextran is taken up by liver and spleen;[23,24] when the animals were killed 6 months after iron-dextran overload, even larger quantities of iron were found in the liver.[24] After intravenous injection of radiolabelled iron dextran in man, more radioactivity was found in the liver than in any other organ at the end of the study period (4 to 6 weeks).[25,26] Our study shows that there is a failure of mobilisation of hepatosplenic iron to the bone marrow in this setting and that hepatosplenic iron overload may persist even in the face of bone-marrow iron depletion.

Our data raise serious questions about the appropriateness of intravenous iron-dextran therapy for treatment of iron deficiency in dialysis patients. They show that marrow iron cannot be replenished by intravenous iron dextran without incurring serious hepatic iron overload and the risk of liver injury.

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Correspondence should be addressed to M. A., Director, Division of Pathology, Immunology, and Laboratories, Holy Name Hospital, 718 Teaneck Road, Teaneck, New Jersey 07666, U.S.A.

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MOTION SICKNESS, GINGER, AND PSYCHOPHYSICS

DANIEL B. MOWREY

Department of Psychology, Brigham Young University, Provo, Utah

DENNIS E. CLAYSON

Department of Psychology, Mount Union College, Alliance, Ohio, U.S.A.

Summary The effects of the powdered rhizome of *Zingiber officinale* on the symptoms of motion sickness were compared with those of dimenhydrinate and placebo in 36 undergraduate men and women who reported very high susceptibility to motion sickness. Motion sickness was induced by placing the blindfolded subject in a tilted rotating chair. Measurements of perceived degree of gastrointestinal distress were reported every 15 s for up to 6 minutes by means of psychophysical methods. *Z. officinale* was superior to dimenhydrinate in reducing motion sickness.

Introduction

Lewis and Lewis,[1] in their review of the therapeutic properties of plants, included the fluid extract of the rhizome of ginger (*Zingiber officinale*) among the natural products which mitigate symptoms of gastrointestinal distress, thus continuing a tradition that dates back at least as far as 1597.[2]

Traditionally, investigations of ginger root have used fluid extracts.[3] Our preliminary study, however, suggested that powdered whole root may have pronounced therapeutic effects. The purpose of our study was to determine whether the powdered whole root was effective in suppressing the gastrointestinal symptoms related to motion sickness.

We used the psychophysical techniques of Stevens,[4] who found that, when subjects were asked to indicate with

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numbers how intense a stimulus appeared, there was a high degree of consistency among the subjects in the relation between the numbers assigned and the physical intensity of the stimulus. The ratios between numbers assigned by subjects and the ratios between stimulus intensities are proportional to each other, averaged across the subjects.

The relation between equal intensity ratios and equal sensation ratios is a power function, of the form:

$$S = aI^b$$

where a and b are exponents characteristic for different sensory continua, S is the psychological magnitude, and I is the physical magnitude of the stimulus. The greater the value of b, the stronger the impact of the stimulus I on perception. Power functions give straight lines on logarithmic plots; the slope of such a line gives the value of exponent b.

Some of the sensations in motion sickness arise in the visceral organs and are not, therefore, directly measurable: the sensations are nevertheless directly accessible to the subject, much as the perception of brightness is the private experience of the subject. The subject should therefore be able to assign numbers that reflect gastrointestinal sensations.

Subjects and Methods

Subjects

18 male and 18 female paid volunteers aged 18–20 years were selected from undergraduate classes on the basis of self-rated extreme or very high susceptibility to motion sickness, reported in a questionnaire asking about susceptibility to ten common health disorders. 3 extremely susceptible and 3 very highly susceptible subjects of each sex were randomly assigned to each of three groups. The subjects were unaware of the purpose of the experiment until after it was completed, when they were given a detailed explanation, and they were paid.

Methods

Apparatus.—A motor-driven revolving chair was used to produce motion sickness. The chair's rotational speed was varied between 4 and 17 rpm. One of its legs was 6·5 cm longer than the other two to add a vertical component to the rotation.

Drugs.—Subjects were given one of the following: 100 mg dimenhydrinate ('Dramamine'); two gelatin capsules (940 mg) of the powdered rhizome of *Z. officinale;* or two capsules of powdered chickweed herb *(Stellaria media),* which served as a placebo control.

Procedure.—Subjects were asked to ingest either dimenhydrinate or "two capsules of a mixture of harmless garden herbs". None of the subjects recognised dimenhydrinate as dramamine or connected any of the three substances with motion sickness. They were instructed that the purpose of the experiment was to assess the effect of the compound on the performance of three simple tasks. The aim of the first two tasks was to give the subjects experience with the psychophysical method; they were asked to estimate the lengths of several lines and then the areas of circles. Each subject completed the first two tasks and was then blindfolded, led to the rotating chair which had previously been concealed, and asked to sit down and to lay his or her head on the right shoulder. The following instructions were read, directing the subjects to give magnitude estimations when so asked.

"In a moment the chair will begin to revolve slowly. Let us see if you can do the same thing with the feelings in your stomach as you did with the lines and circles. Every few seconds, I will ask you to tell me how intense the feelings in your stomach are by assigning numbers to them. It is important that you pay strict attention to just your stomach. Do not confuse dizziness in your head with feelings in the stomach. They are not the same thing. Think just about your stomach when giving me numbers. Assign successive numbers in such a way that they reflect your subjective impressions. There is no limit to the range of numbers that you may use. You may use whole numbers, decimals, or fractions. Try to make each number match the intensity of stomach feeling as you perceive it. Any questions?"

The time between the subject swallowing the pills and the chair beginning to rotate was 20–25 min. Every 15 s the experimenter asked for and recorded a magnitude estimation. The experiment was stopped if the subject vomited; or if the subject requested that it be terminated; or if there was a three-fold increase in the magnitude estimation on three consecutive occasions; or after 6 min.

TIMES IN REVOLVING CHAIR AND POWER FUNCTIONS FOR MAGNITUDE ESTIMATIONS IN THREE TREATMENT GROUPS

—	Placebo	Dimenhydrinate	*Z. officinale*
Mean±SEM time in chair (range; s)	90·0±12·2 (45–180)	216·2±10·0 (165–270)	335·8±8·2 (285–360)
Power function above knee (95% CI)	3·80 (3·73)	3·40 (0·86)	3·87 (1·01)
r^2	0·90	0·93	0·94
Power function below knee (95% CI)	1·38 (0·35)	0·81 (0·18)	0·59 (0·10)
r^2	0·94	0·94	0·92

95% CI = 95% confidence interval.

Results

The power functions for the first two practice tasks for all three groups were identical to the previously identified values for these tasks.[4]

No subject, while in the revolving chair, asked to stop before other criteria for stopping were reached, although 3 subjects in the placebo group vomited.

Geometric means for each 15 s period for each group were computed separately according to D'Amato's procedure.[5] The geometric mean magnitude estimations of the placebo group increased most rapidly, followed by those of the dimenhydrinate group, while those of the *Z. officinale* group rose only slowly (fig. 1). A median test[6] showed that differences between the mean magnitude estimations of the three groups were significant (χ^2 [2] = 7·39; $p<0·05$).

None of the subjects in the placebo and dimenhydrinate groups was able to stay in the chair for 6 min (fig. 1), whereas half of the subjects in the *Z. officinale* group stayed for the full time. Differences between the groups in the mean times in the chair were significant (F [2, 33] = 142·32; $p<0·001$); each group differered significantly from the other two (Neuman–Keuls test). The means and ranges for the data are listed in the table.

No single power function described the entire set of data for any one group, but pairs of power functions were determined by maximising the average r^2 for a least-squared regressional fit. The pairs of power functions formed bends or "knees" (fig. 2); these have been found in several other situations.[7,8]

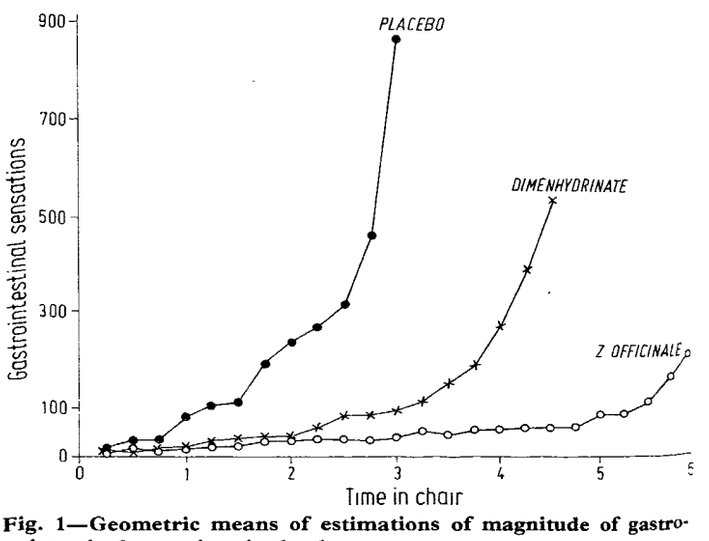

Fig. 1—Geometric means of estimations of magnitude of gastrointestinal sensations in the three treatment groups.

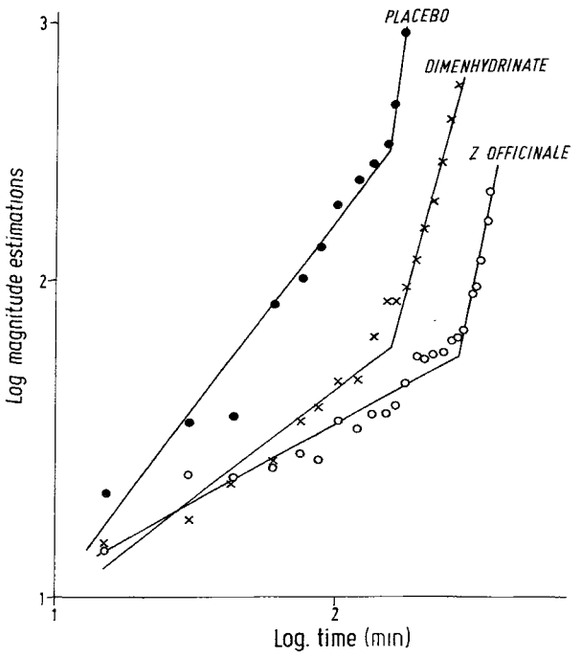

Fig. 2—Logarithmic plots of fig. 1 curves.

Slopes correspond to exponents of power functions.

The table shows the power functions above and below the knees; above the knees the power functions overlap the 95% confidence intervals of the others, but below the knee each power function lies outside the confidence intervals of the other two. The power of the functions above the knee was not the result of stopping the experiment when there was a three-fold increase in the magnitude estimation on three successive occasions; this would have produced a theoretical power of 6·31. Nor was the power of these functions due to the unequal sample sizes in the later time periods.

Discussion

Z. officinale in powdered form was superior to dimenhydrinate in preventing the gastrointestinal symptoms of motion sickness.

The phenomenon of the knee in the power function has been found in other situations.[7,8] One power function describes the relation to a point at which a new or additional sensory mechanism begins to exert a different effect (or at which some sensory information may be sacrificed) and the second power function is created at that point. In this case the two power functions may describe steadily increasing gastrointestinal distress reaching a threshold at which qualitatively distinct sensory receptors are stimulated and begin to relay their information to other integrative centres in the nervous system. These new sensory data may be the preliminaries to or part of the vomiting reflex.

Vomiting due to motion sickness is commonly believed to arise through stimulation of the receptors in the labyrinth, from which impulses are transmitted, either directly or by way of the vestibular nuclei, through the cerebellum, by way of the uvula vermis and the nodule to the chemoreceptor site near the fasciculus solitarius and area postrema. Impulses are then transmitted centrally to the vomiting centre in the dorsolateral reticular formation.[9] If this was the only mechanism, vomiting would eventually take place without concomitant nausea. Vomiting may occur in the absence of any prior sensations.[10]

The sensation of nausea due to motion has central nervous system (CNS) as well as gastrointestinal components. A nausea centre is located in the area of the medulla close to or perhaps part of the vomiting centre but distinct from it.[9] Thus nausea and vomiting are mediated by distinct CNS nuclei. Connections between the labyrinth and the visceral organs by way of the medullary reticular formation and the vagus have been postulated.[11–16] Nausea sensations probably occur at lower levels of labyrinthine stimulation than are required to initiate enough activity in the vomiting centre to produce the vomiting reflex itself.

The knee in the power function may reflect the point at which the vomiting centre is activated and, although perhaps providing no direct sensory input itself, begins to modify sensations mediated by this centre. Although each of the three functions was displaced in time, there was no statistical difference between the slopes of the functions above the bend. It therefore took longer in the *Z. officinale* group for the point of additional input to be reached, but once the vomiting centre was activated, the sensations progressed in the same way in all groups. The significant differences between the placebo group and the *Z. officinale* and dimenhydrinate groups before the knee, however, indicate a powerful action by these substances on the nausea-inducing mechanism in motion sickness.

Z. officinale and dimenhydrinate (an antihistamine) probably operate at different levels or by different mechanisms. In motion sickness antihistamines block the transmission of evoked potentials at the second-order vestibular synapse by modifying the input from the reticular formation,[17,18] but it is unlikely that powdered ginger root acts at the CNS level. The aromatic and carminative properties of ginger[3,19] and its possible absorbent properties[20] suggest that ginger ameliorates the effects of motion sickness in the gastrointestinal tract itself. It may increase gastric motility and absorb neutralising toxins and acids, so effectively blocking gastrointestinal reactions and subsequent nausea feedback.

Correspondence should be addressed to D. E. C., Department of Psychology, Mount Union College, Alliance, Ohio 44601, U.S.A.

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