Salivary Secretion and Seasickness Susceptibility

CARLOS R. GORDON, M.D., D.Sc., YAEL JACKMAN, M.D., HANNA BEN-ARYEH, D.Sc., ILANA DOWECK, M.D., ORNA SPITZER, M.Sc., RAYMONDE SZARGEL, M.Sc., and AVI SHUPAK, M.D.

GORDON CR, JACKMAN Y, BEN-ARYEH H, DOWECK I, SPITZER O, SZARGEL R, SHUPAK A. *Salivary secretion and seasickness susceptibility*. Aviat. Space Environ. Med. 1992; 63:356–9.

The salivary flow rate and composition of 2 groups of 31 subjects, one group at each extreme of the seasickness susceptibility scale, were compared. No significant differences were found between the two groups in flow rates and electrolyte concentrations of whole resting and stimulated saliva. Amylase activity and rate of secretion in resting saliva were significantly higher in subjects susceptible to seasickness as compared with nonsusceptible subjects. Also, the total protein rate of secretion in resting saliva was significantly higher in the susceptible group. The present findings could be explained in terms of higher sympathetic tone in subjects susceptible to seasickness, and salivary amylase levels might be recommended as an additional parameter in the evaluation of seasickness susceptibility.

SEASICKNESS is a well recognized form of motion sickness. Although the underlying neurophysiologic mechanism of motion sickness is still obscure, the neural mismatch and sensory rearrangement theory is currently accepted as an explanation of motion sickness etiology and pathogenesis (15,17,18). According to this theory, motion sickness occurs in all situations in which the motion inputs of vestibular and non-vestibular proprioception, and vision, are in conflict with each other and with what is expected on the basis of previous natural motion experiences. Whatever the provocative situation, the most frequent signs and symptoms of motion sickness are pallor, cold sweating, nausea, vomiting, salivary changes, and drowsiness (7,18).

In contrast with the classic concept of increased salivation during motion sickness (7,18), we recently reported a significant decrease of salivary flow rate in subjects exposed to both experimental motion sickness condition in a rotatory chair (5), and to a real seasickness situation (6). In both studies the previous motion seasickness susceptibility was unknown, and motion sickness severity was scored during the provocative motion exposure. A positive correlation was found between total salivary protein concentration and motion sickness, and seasickness severity. This correlation was detected before, as well as during, actual exposure to motion sickness situations. These findings encouraged us to examine further the relationship between salivary variables and motion sickness susceptibility.

The purpose of the present study is to evaluate the relationship between saliva and seasickness susceptibility, by comparing highly susceptible with nonsusceptible subjects.

MATERIALS AND METHODS

The subjects were 2 groups of 31 healthy males each (susceptible and nonsusceptible to seasickness), obtained from a naval crew population. Their ages ranged between 18 and 20 years. All subjects had at least 3 months experience at sea. Susceptibility to seasickness was determined using a motion sickness questionnaire concerning the past and present history of motion sickness (18) and a seasickness questionnaire adopted from Wiker *et al.* (22,23) dealing with actual seasickness severity during sailing. The validity and reliability of this questionnaire were proved to be high in a seasickness survey conducted by the U.S. Coast Guard (23). Based on self-reported symptoms, seasickness is rated on a scale from 0 to 7. Our susceptible group included 31 highly susceptible subjects: 7 points on the scale cate-

From the Motion Sickness and Human Performance Laboratory, Israel Naval Hyperbaric Institute, Haifa (C. R. Gordon, I. Doweck, O. Spitzer, and A. Shupak); Laboratory of Oral Biology, Dept. of Oral Surgery, Rambam Medical Center and Faculty of Medicine, Technion—Israel Institute of Technology, Haifa (Y. Jackman, H. Ben-Aryeh, R. Szargel); Dept. of Neurology, Beilinson Medical Center, Petah Tiqva, Sackler School of Medicine, Tel Aviv University (C. R. Gordon).

This article was received for review in September and revised in October 1991. The revised manuscript was accepted for publication in October 1991.

Address reprint requests to C. R. Gordon, M.D., D.Sc., who is a Lecturer in Neurology, Dept. of Neurology, Beilinson Medical Center, Petah Tiqva 49100, Israel. He is also a Lecturer at the Sackler School of Medicine, Tel Aviv University, Israel.

gorization, (subjects regularly vomiting during sailing). The nonsusceptible group included 31 nonsusceptible and slightly susceptible subjects: 0 to 2 point categorization (subjects sometimes slightly suffering from minor signs of motion sickness during sailing). This categorization was further validated using peer questionnaires.

Subjects were completely drug-free for at least 72 h before the study. Resting and stimulated whole saliva was collected by the spitting method, at least 1 h after meals (1,4,9,16). Subjects were seated comfortably in a light-temperature-noise controlled room and asked to spit into a test tube for 10 min (resting saliva). After a 15-min rest, stimulated saliva was collected by applying a cotton swab immersed in a 2% citric acid solution to the sides of the tongue, every 30 s, during additional 10 min.

Salivary volume was measured with a 0.1 ml scale. Sodium and potassium concentrations were measured by flame photometry, calcium and magnesium by atomic absorption, total protein by the method of Lowry *et al.* (13), and amylase by the Phadebase amylase test. Statistical analysis was carried out with SPSS-11 software and a PDP 11/23 computer.

RESULTS

Table I summarizes the mean salivary flow rates and electrolyte concentrations of resting and stimulated saliva for the two study groups. No significant differences in salivary flow rate, sodium, potassium, calcium or magnesium concentrations were found between the two groups.

Table II summarizes the mean salivary protein and amylase concentrations and rate of secretion in the two study groups. Total protein concentration was higher in both resting and stimulated saliva in the susceptible group as compared to the nonsusceptible group; however, these differences were not statistically significant. Also, the rate of protein secretion in resting saliva was higher in the susceptible group and the difference was statistically significant ($p < 0.012$). The rate of protein secretion in stimulated saliva was also slightly higher in the susceptible group; however, the difference was not statistically significant.

Amylase activity and rate of secretion in resting saliva were significantly higher in the susceptible group ($p < 0.017$ and $p < 0.001$, respectively). The amylase activity and rate of secretion in stimulated saliva were also higher in the susceptible group, but the differences only bordered on statistical significance ($p < 0.162$ and $p < 0.170$, respectively).

Pearson's correlation coefficients were calculated between salivary flow, protein and amylase, and are summarized in Table III.

A significant positive correlation was found between amylase and protein concentration of both resting and stimulated saliva in the nonsusceptible ($r = 0.745$, $p < 0.001$ and $r = 0.420$, $p < 0.01$, respectively) and also in the susceptible group ($r = 0.679$ $p < 0.001$ and $r = 0.368$, $p < 0.025$, respectively). Negative correlations were found between resting salivary flow rate and protein and amylase concentrations, but statistical significance was found only in the nonsusceptible group. These correlations disappeared in stimulated saliva.

DISCUSSION

The present results demonstrate significant difference in salivary amylase levels in subjects at the two extremes of the seasickness susceptibility scale. The amylase activity and rate of secretion in resting saliva were significantly higher in subjects susceptible to seasickness as compared with nonsusceptible subjects.

We previously reported a positive correlation between salivary protein concentration and motion sickness and seasickness severity (5,6). Based on this finding we postulated a possible difference between protein levels in subjects who were susceptible and nonsusceptible to seasickness. Indeed, in the present study a higher protein concentration and rate of secretion were found in the susceptible group; however, this difference was significant only for the protein secretion in resting saliva. No significant differences were found in salivary flow rate and electrolytes between the two groups.

Although sympathetic and parasympathetic nerves of salivary glands function in an integrated manner, the secretion of amylase is regulated mainly by sympathetic innervation (3,20). Sympathetic activity modulates the protein content of saliva by increasing exocytosis from acinar cells (2,3). Our results might be tentatively explained in terms of high sympathetic tone in subjects susceptible to seasickness. The phys-

TABLE I. SALIVARY FLOW RATES AND ELECTROLYTE CONCENTRATIONS OF RESTING (−) AND STIMULATED (+) SALIVA FOR THE TWO STUDY GROUPS.

	Type of saliva	No.	Susceptible to seasickness	No.	Nonsusceptible to seasickness	p*
Flow rate	−	31	0.54 ± 0.34	31	0.43 ± 0.31	NS
(ml/min)	+	31	2.29 ± 0.86	31	2.20 ± 0.94	NS
Sodium	−	30	4.4 ± 2.5	30	3.8 ± 2.3	NS
(mEq/L)	+	30	15.3 ± 10.0	30	18.7 ± 12.5	NS
Potassium	−	30	20.7 ± 5.6	31	20.6 ± 5.7	NS
(mEq/L)	+	30	17.2 ± 4.2	30	18.3 ± 3.4	NS
Calcium	−	30	3.8 ± 2.0	28	4.4 ± 3.0	NS
(mg%)	+	30	6.3 ± 2.7	31	5.8 ± 1.6	NS
Magnesium	−	30	0.40 ± 0.22	31	0.42 ± 0.33	NS
(mEq/L)	+	30	0.30 ± 0.28	30	0.27 ± 0.20	NS

Values shown are means ± S.D.
* NS = not significant (unpaired *t*-test between groups).

TABLE II. SALIVARY PROTEIN AND AMYLASE CONCENTRATIONS AND RATE OF SECRETION FOR THE TWO STUDY GROUPS.

	Type of saliva*	No.	Susceptible to seasickness	No.	Nonsusceptible to seasickness	p†
Protein	−	31	181 ± 80	31	155 ± 65	NS
(mg/ml)	+	30	130 ± 77	31	113 ± 46	NS
Amylase	−	29	3761 ± 2855	31	2222 ± 1841	0.017
(IU × 10^2/L)	+	29	3673 ± 2633	30	2788 ± 2125	NS
Protein‡	−	31	92 ± 63	31	58 ± 39	0.012
(μg/min)	+	30	312 ± 284	31	252 ± 149	NS
Amylase‡	−	29	1800 ± 1430	31	757 ± 508	0.001
(IU × 10^{-1}/min)	+	29	8338 ± 6078	30	6182 ± 5840	NS

Values shown are means ± S.D.
* − resting saliva; + stimulated saliva.
† NS = nonsignificant (unpaired t-test between groups).
‡ The rate of protein and amylase secretions for each subject was calculated as concentration × flow rate.

TABLE III. PEARSON'S CORRELATION COEFFICIENTS BETWEEN SALIVARY FLOW, PROTEIN AND AMYLASE CONCENTRATIONS FOR THE TWO STUDY GROUPS.

	Resting Saliva		Stimulated Saliva	
	Protein (concentration)	Amylase (activity)	Protein (concentration)	Amylase (activity)
Susceptible to seasickness				
Resting flow rate	r = −0.230 p = 0.107	r = −0.283 p = 0.068	—	—
Protein (concentration)	—	r = 0.679 p < 0.001*	—	—
Stimulated flow rate	—	—	r = 0.262 p = 0.081	r = −0.058 p = 0.383
Protein (concentration)	—	—	—	r = 0.368 p = 0.025*
Nonsusceptible to seasickness				
Resting flow rate	r = −0.476 p = 0.003*	r = −0.370 p = 0.020*	—	—
Protein (concentration)	—	r = 0.745 p < 0.001*	—	—
Stimulated flow rate	—	—	r = 0.096 p = 0.304	r = 0.060 p = 0.377
Protein (concentration)	—	—	—	r = 0.420 p = 0.010*

* Statistically significant.

iological significance of the present results and the possible use of amylase as an additional parameter in the prediction of motion sickness susceptibility require further investigation.

Many efforts have been made to find objective physiological parameters which might usefully be employed as predictors of motion sickness susceptibility. Unfortunately, examination of vestibular function by caloric or rotational tests has not been found to be useful in differentiating between subjects susceptible or nonsusceptible to motion sickness (18,19). Vestibulo-autonomic reactions during provocative motion sickness conditions have been relatively poorly investigated by measuring pallor, galvanic skin response, cardiovascular changes and gastrointestinal motility (8,11,12,21). Hypersalivation, one of the most frequent signs of motion sickness, has been erroneously reported in man, evaluated by subjective reports only (7,18). To the best of our knowledge, our previous (5,6) and present study and two recent reports (10,14) constitute the first attempts to objectively characterize the changes in salivary secretion associated with the motion sickness syndrome. These studies support the assumption that examination of salivary glands' secretion could serve as a model to study vestibulo-autonomic activity associated with motion sickness syndrome.

Further studies in subjects with different susceptibilities to seasickness, and measurements of separate salivary glands' secretion during different motion conditions are indicated in order to clarify the suggested association between salivary amylase and motion sickness syndrome.

ACKNOWLEDGMENTS

This article was based on a thesis by Yael Jackman, M.D., submitted to the Faculty of Medicine, Technion-Israel Institute of Technology, in partial fulfillment of the requirements of the M.D. degree.

REFERENCES

1. Ben Aryeh H, Shalev A, Szargel R, Laor A, Laufer D, Gutman D. The salivary flow rate and composition of whole and parotid resting and stimulated saliva in young and old healthy subjects. Biochem. Med. Metab. Biol. 1986; 36:260–5.

2. Brobeck JR. Best and Taylor's physiological basis of medical practice, 10th ed. Baltimore: Williams and Wilkins; 1981:24–37.
3. Garret JR. Innervation of salivary glands. Neurohistological and function aspects. In: Sreebny LM, ed. The salivary system. New York: Dept. of Oral Biology and Pathology, State University N.Y.; 1987:69–93.
4. Gordon CR, Ben-Aryeh H, Attias J, Szargel R, Gutman D. Effect of transdermal scopolamine on salivation. J. Clin. Pharmacol. 1985; 25:407–12.
5. Gordon CR, Ben-Aryeh H, Szargel R, Attias J, Rolnick A, Laufer D. Salivary changes associated with experimental motion sickness condition in man. J. Auton. Nerv. Syst. 1988; 22:91–6.
6. Gordon CR, Ben-Aryeh H, Szargel R, Attias J, Rolnick A, Laufer D. Salivary changes associated with seasickness. J. Auton. Nerv. Syst. 1989; 26:37–42.
7. Graybiel A, Wood CD, Miller EF, Cramer DB. Diagnostic criteria for grading the severity of acute motion sickness. Aerosp. Med. 1968; 39:453–5.
8. Graybiel A, Lackner JR. Evaluation of the relationship between motion sickness symptomatology and blood pressure, heart rate and body temperature. Aviat. Space Environ. Med. 1980; 51:211–4.
9. Gutman WH, Ben-Aryeh H. The influence of age on salivary content and rate flow. Int. J. Oral Surg. 1974; 3:314–7.
10. Igarashi M, MacDonald S, Chae SY, Plishker GA, Kohl RL. Sodium concentration in saliva along the time course of experimental Coriolis sickness. Acta Otolaryngol. 1989; 107:485–8.
11. Isu N, Koo J, Takahashi N. Changes of skin potential level and of skin resistance level corresponding to lasting motion discomfort. Aviat. Space Environ. Med. 1987; 58:136–42.
12. Johnson WH, Jonkees LBW. Motion sickness Part 1: Aetiology and autonomic effects. In: Kornhuber HH, ed. Handbook of sensory physiology (Vol. VI/2), Vestibular system. New York: Springer; 1974:389–404.
13. Lowry DH, Rosebrough NJ, Farr AL, Randall RJ. Protein determination with the Folin phenol reagent. J. Biol. Chem. 1951; 193:65–275.
14. MacDonald S, Igarashi M, Henley CM, Reschke MF. Changes in the total protein concentration of saliva during experimental motion sickness (Abstract). Aviat. Space Environ. Med. 1989; 60:493.
15. Money KE. Motion sickness. Physiol. Rev. 1970; 50:1–39.
16. Navazesh M, Christensen CM. A comparison of whole-mouth resting and stimulated salivary measurement procedures. J. Dent. Res. 1982; 61:1158–62.
17. Reason JT. Motion sickness: a special case of sensory rearrangement. Advancement Sci. 1970; 26:386–93.
18. Reason JT, Brand JJ. Motion sickness. London: Academic Press; 1975.
19. Schwarz V, Henn MD. Vestibular habituation in student pilots. Aviat. Space Environ. Med. 1989; 60:755–61.
20. Speirs RL, Herring J, Cooper D, Hardy CC, Hind CRK. The influence of sympathetic activity and isoprenaline on the secretion of amylase from the human parotid gland. Arch. Oral. Biol. 1974; 19:747–52.
21. Stern RM, Koch KL, Stewart WR, Lindbland IM. Spectral analysis of tachygastria recorded during motion sickness. Gastroenterology 1987; 92:92–7.
22. Wiker SF, Kennedy RS, McCauley ME, Pepper RL. Susceptibility to seasickness: influence of hull design and steaming direction. Aviat. Space Environ. Med. 1979; 50:1046–51.
23. Wiker SF, Kennedy RS, McCauley ME, Pepper RL. Reliability, validity and application of an improved scale for assessment of motion sickness severity. Washington, DC: U.S. Dept. of Transportation, U.S. Coast Guard, Office of Research and Development, 1979; Report No: CG-D-29-79.