**MODIFICATION OF HUMAN GASTRIC ACID SECRETION
WITH OPERANT-CONDITIONING PROCEDURES¹**

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In an attempt to control gastric acid secretion with operant-conditioning techniques, four normal women were given visual feedback on gastric pH plus money reinforcers. When money was made dependent on increased secretion in a differential-reinforcement-of-high-rates schedule, the rate of secretion of three of the four subjects increased to three times baseline. When money was then made dependent on decreased secretion in a differential-reinforcement-of-other-behaviors schedule, the rate of secretion of these three subjects returned to baseline levels. Heart rate, respiratory frequency, abdominal electromyographic activity, and stomach motility (measured by the electrogastrogram method) were not consistently correlated with acid secretion across subjects, although individual subjects showed substantial correlations between acid secretion and one or more other physiological response.

DESCRIPTORS: gastric acid secretion, operant conditioning of gastric acid secretion, gastric pH, biofeedback, differential reinforcement of high rate to increase gastric acid secretion, DRO to reduce gastric acid secretion, visceral learning

A variety of autonomic responses have been modified with operant-conditioning procedures (Miller, 1969; Shapiro and Schwartz, 1972). Miller (1969) and others have called attention to the possible value of these techniques in the treatment of psychophysiologic disorders. Successful clinical applications have included elimination of ruminative vomiting (Lang and Melamed, 1969), reduction in cardiac arrhythmias (Weiss and Engel, 1971), and reduction of blood pressure in essential hypertension (Benson, Shapiro, Tursky, and Schwartz, 1971; Elder, Ruiz, Deabler, and Dillenkoffer, 1973).

Welgan (1974) reported an attempt to condition by operant means increased gastric pH in duodenal ulcer patients. Gastric secretions were continuously aspirated and pH was measured outside the body. Subjects served in a single session, and 15-min periods of visual and auditory feedback alternated with 15-min periods of rest. Group data were generally consistent with the hypothesis that feedback plus instructions reduced gastric acidity, but did not provide definitive support for this hypothesis. In an earlier study, Gorman and Kamiya (1972) measured pH within the stomach during three sessions, in which instructions to increase pH alternated with instructions to decrease pH, accompanied by auditory feedback. Group data demonstrated a significant difference between increase and decrease conditions.

Technical problems and the equivocal nature of some of these data underscore the need for additional studies. The technical difficulties include the absence of immediate feedback in Welgan's (1974) study and the nonlinear relation of intragastric pH to acid secretion in Gorman and Kamiya's (1972) study. Continu-

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ously aspirating from a stomach tube introduces relatively long delays between secretion and measurement, especially as the tube tends to clog when the stomach is empty. Although measuring pH within the stomach is more immediate, it may be less valid as a measure of acid secretion for the following reasons: acid is secreted at a constant concentration (Cummins, 1973), but the contribution of a given amount of acid secretion to intragastric pH is determined by the volume of fluid already in the stomach. Moreover, pH is logarithmically related to acid concentration, so that a change from pH3 to pH2 reflects 10 times as much difference in acid concentration as a change from pH4 to pH3 (Gambescia, Krawiec, Desiderio, and Polish, 1967).

The current investigation overcame these difficulties. Intragastric pH was used to provide immediate feedback and reinforcement to the subjects; in order to measure more validly acid secretion, the contents of the stomach were repeatedly neutralized to pH7. Titration to this endpoint rendered the measurement of acid secretion independent of volume changes, since the amount of sodium bi carbonate required was taken as the dependent measure of acid secretion.

METHOD

Subjects

Four female volunteers (ages 21 to 28 yr), with no history or symptoms of gastrointestinal pathology, were paid \$10 for each baseline session and a varying amount that depended on performance but that averaged about \$10 for each conditioning session. Additional payment of up to \$200 was available for finishing the study (approximately five months) without missing more than four sessions.

Apparatus

Subjects swallowed a plastic tube (Figure 1) containing a pH electrode (Beckman 39042) and two smaller tubes, one used to inject sodium bicarbonate into the stomach and the other to

inject water if the side holes became clogged with mucus. The electrode tip was enclosed in a plastic cuff (8 mm outside diameter) to prevent it from becoming engulfed in the stomach lining. The reference for the pH electrode was a fiber junction electrode with its tip immersed in a pan of saturated potassium chloride solution in which the subject held one hand (Rovelstad, Owen, and Magath, 1952).

The pH electrode was connected to a high-impedance amplifier whose output was recorded on a polygraph. Standard buffer solutions were used to calibrate the system. The output of the polygraph amplifier drove a volt meter that provided visual feedback to the subject and

Fig. 1. Left, pH probe. Letter a, polyethylene tube used to infuse sodium bicarbonate into stomach (cut off flush with cuff in practice); b, hole in cuff to allow stomach contents to contact pH electrode; c, polyethylene tube used to wash out cuff with water; d, plug in end of cuff to facilitate washing outside holes. Right, pH electrode without cuff.

drove an electronic circuit that closed a relay whenever pH decreased by a predetermined amount.

Subjects faced a display panel with a counter that accumulated reinforcements, a white light that flashed whenever the counter advanced, and red and green stimulus lights. During conditioning sessions, a meter on the panel showed relative changes in intragastric pH.

Method of Measuring Acid Secretion

Sodium bicarbonate (1 Normal) was injected to neutralize the stomach contents to pH7. Gastric acid secretion then caused pH to decrease at a rate that depended on the rate of acid secretion, and subjects received reinforcement for appropriate small changes in the rate of pH decrease. Each time stomach pH fell to 2, additional sodium bicarbonate was injected to titrate the pH back to 7. The amount of sodium bicarbonate required repeatedly to neutralize the stomach contents, expressed as milliequivalents (mEq) per minute, was the dependent measure of acid secretion.

Occasionally, recorded pH showed large, rapid fluctuations, indicating that the pH electrode was not in contact with fluid, or recorded pH failed to show any change for much longer than would be expected for that subject (as judged by the experimenter), indicating the electrode tip was clogged with mucus or engulfed in the gastric mucosa. When either occurred, 10 to 20 cc of water was injected into the cuff. If this failed to correct the problem, the tube containing the pH electrode was raised or

lowered slightly. Amount of water injected into the stomach and number of times electrode position was adjusted were recorded.

A control experiment was conducted to compare the technique of titrating acid secretion in the stomach to the more traditional technique of aspirating and titrating outside the body. Two 1-hr observations of basal secretion and two 1-hr observations of histalog-stimulated secretion (0.5 mg intramuscular) for each method were compared in three subjects. Data are given in Table I. Rate of secretion varied as much between measurements taken with the same method as it did between different methods, and one method did not give results systematically different from the other. This held both for basal secretion (low rate of secretion) and histalog-stimulated secretion (high rate of secretion).

Experimental Design

The number of baseline sessions ranged from five to 13, depending on the stability of basal secretion from session to session. After baseline, increased acid secretion was reinforced until acid secretion rose above baseline levels for several consecutive sessions. Decreased acid secretion was then reinforced.

Increase training consisted of a differential-reinforcement-of-high-rates (DRH) schedule in which reinforcement was presented only if intragastric pH decreased by a specified amount (0.1 pH unit typically) within a 10-sec trial. If this criterion was not met within 10 sec, pH had to decrease by this amount within the next 10-sec trial. If the criterion was met in less than 10 sec,

Table 1
Comparison of pH Method and Aspiration Method of Measuring Gastric Acid Secretion

Subject	Session	Basal mEq/hr		Histalog mEq/hr	
		pH method	Aspiration	pH method	Aspiration
B.W.	Initial Study	6.27	4.37	25.73	21.68
	Replication	3.07	4.65	36.70	27.64
C.D.	Initial Study	1.20	0.91	11.00	14.60
	Replication	9.80	1.87	28.00	13.50
R.R.	Initial Study	3.90	3.52	18.20	25.21
	Replication	4.50	2.75	22.60	7.64

the reinforcement counter advanced and a new trial started immediately.

Decrease training consisted of a differential-reinforcement-of-other-behavior (DRO) schedule in which reinforcement was presented only if a criterion interval of time passed with no decrease in pH. A 2-sec interval was used at the beginning of training, and was gradually increased to 5 sec.

The subject was told before each session what the contingency of reinforcement was and how much money each successful trial was worth. Size of the reinforcer was varied from session to session (one to three cents) depending on the contingency and on past performance. The aim was to make expected earnings equal to \$10 per session.

Before the experiment, subjects were taught to swallow a stomach tube during three or more 1-hr sessions that served to habituate any unconditioned effects of swallowing a tube. Sessions occurred at least 8 hr after the subject's last meal to avoid any stimulation of acid secretion by food. Subjects' stomachs were emptied by hand aspiration at the beginning of each session; if food was present, the session was not conducted. Sessions were held at the same time each day to avoid variations in acid secretion attributable to the circadian rhythm of acid secretion (Moore and Englert, 1970). Subjects lay in bed on their left side during sessions to reduce gastric emptying. Sessions lasted 105 min. The experimenter stood in an adjacent room out of the subject's sight.

Controls for Mediation

Abdominal muscle EMG (electromyographic) activity and respiration were recorded in three subjects to evaluate the most likely sources of skeletal muscle mediation. To assess the extent of possible cognitive mediation of acid secretion, one subject was instructed (a) to think about food, (b) to think about whatever she liked that she believed would increase acid secretion, and (c) to look at pictures of prepared food while

acid secretion was measured. This occurred before training.

Gastric acid secretion might have been stimulated by putting too much water into the stomach and distending it (Sugawara, Isaza, Curt, and Woodward, 1970). To assess whether this could account for observed changes in acid secretion, the correlation of amount of water added with acid secretion was calculated. The tactile stimulation involved in adjusting the position of the pH electrode might also have stimulated acid secretion. This was assessed by calculating the correlation of movements of the pH electrode with acid secretion.

To determine whether the observed changes in acid secretion were part of a generalized autonomic arousal, the correlations of acid secretion with heart rate and gastric motility, as measured by the electrogastrogram (Russell and Stern, 1967), were calculated. The electrogastrogram measures slow electrical potentials generated by the stomach, which can be recorded from a skin surface electrode over the antrum.

RESULTS

The data for each subject are reported separately below because each subject was treated as a separate experiment and procedures were varied from subject to subject.

Subject C.D.

The baseline rate of secretion, depicted in Section A of Figure 2, averaged 0.0373 mEq/min (range: 0.0240 to 0.0629). There was no tendency for the rate of secretion to increase or decrease systematically across baseline sessions, suggesting that any unconditioned effects of swallowing a tube had habituated by the time baseline sessions began.

The effects of reinforcing secretion on a DRH schedule are depicted in Section B of Figure 1. The rate of secretion was unchanged for the first three sessions, but increased abruptly in the fourth session and remained well above baseline in the fifth and sixth sessions.

Fig. 2. Subject C.D. A, baseline; B, initial increase (DRH) training with no stimulus light during trials; C, subsequent DRH training with red stimulus light on during trials; D, decrease (DRO) training with green stimulus light on during trials. Ordinate is average rate of sodium bicarbonate infusion required repeatedly to neutralize gastric secretions.

Beginning with the seventh session of increased training, a red stimulus light was introduced during 10-sec trial periods. The effect of this change (Section C of Figure 1) was to decrease secretion to near-baseline levels for five sessions. The rate of secretion then increased well above baseline and remained high. For the last four sessions of increase training, the average rate (0.1225 mEq/min) was more than three times the baseline average.

Section D of Figure 1 shows the effects of

switching to a DRO schedule that made reinforcement contingent on decreased acid secretion. By the fourth session, the rate of secretion was practically nil (0.0066 mEq/min).

Following the third increase-training session, gastric motility, amount of water injected, and number of times the electrode position was adjusted were recorded. Only amount of water added was positively correlated with acid secretion ($r = 0.386$). The multiple correlation of all three measures with acid secretion was 0.4274.

Instructions to increase acid secretion by thinking about food, given before conditioning, had no effect. However, instructions to look at pictures of prepared food were associated with increased secretion in two sessions (0.0910 and 0.1280 mEq/min) but not in a third (0.0223 mEq/min). Instructions to think about whatever the subject believed might increase acid secretion produced no change. These instruction conditions were given at the end of the baseline period.

Subject P.S.

Figure 3 shows no tendency for the rate of secretion to increase or decrease systematically across baseline sessions. The mean rate was 0.0531 mEq/min (range: 0.0196 to 0.0941).

Introduction of the DRH schedule produced no apparent effect for seven sessions. The rate of

Fig. 3. Subject P.S. Baseline, increase (DRH), and decrease (DRO) training. Eleven days separate increase Sessions 13 and 14. M denotes first session following start of menstrual flow. Ordinate is average rate of sodium bicarbonate required repeatedly to neutralize gastric secretions.

secretion then increased gradually to values well above baseline. A period of 11 days intervened between Sessions 13 and 14, but this interruption did not affect the measures taken upon return. The average rate for increase Sessions 8 to 21 was 0.1762 mEq/min, more than three times the baseline average.

During two control sessions, gastric secretions were aspirated and titrated outside the body to provide validity checks on the conditioned increases in secretion. Feedback was not available, but conditions were otherwise similar to DRH training sessions. These sessions occurred between DRH (increase) Sessions 14 and 15 and between 15 and 16 in Figure 3. Values of 0.0839 and 0.1226 mEq/min, both well above baseline, were obtained for these aspiration sessions.

Institution of the DRO (decrease) schedule, shown in Figure 3, was associated with a return to baseline levels during five sessions. This was followed by an abrupt increase. The rate of secretion returned again to baseline but did not fall consistently below baseline.

Analysis of the other measures recorded indicated that across all sessions, amount of water added to the stomach was highly correlated with acid secretion (0.451), as were respiratory rate (0.391) and number of times the position of the electrode was adjusted (0.396). The multiple correlation coefficient of these variables plus motility and EMG with acid secretion was 0.5498. Heart rate correlated 0.444 and gastric motility correlated 0.127 with amount of acid secreted.

Subject C.C.

The average baseline rate, shown in Figure 4, was 0.0193 mEq/min (range: 0.0013 to 0.0280). For the first 25 sessions of increase training, a 15-min timeout period was scheduled at the beginning and end of each session in an attempt to establish control over differential rates of secretion in the same session. This procedure did not increase secretion within 25 sessions. Moreover, secretion was not higher

Fig. 4. Subject C.C. Baseline and increase (DRH) training sessions with 15-min timeouts at beginning and end of session. Timeouts not included in data represented. M denotes first session following start of menstrual flow. Ordinate is average rate of sodium bicarbonate infusion required repeatedly to neutralize gastric secretions.

during the DRH portion of these sessions than during timeout periods.

By contrast, the two subjects previously described had increased acid secretion substantially within 10 sessions when the DRH contingency had been in effect during the entire session. For these reasons, the timeouts were eliminated.

Reinforcing acid secretion for the whole session was not immediately effective, as shown in Figure 5. However, sessions in which the rate of secretion was above the baseline range of variability became increasingly frequent, and for the last six sessions of increase training, the rate of secretion was 0.0629 mEq/min, which was more than three times the baseline average.

Seven sessions of decrease training followed. The DRO contingency was in effect for the

Fig. 5. Subject C.C. Baseline, increase (DRH) training without timeouts, and decrease (DRO) training without timeouts. M denotes first session following start of menstrual flow. Ordinate is average rate of sodium bicarbonate infusion required repeatedly to neutralize gastric secretions.

whole session. By the fifth session, rate of secretion had returned to baseline but not below.

At about the time this subject began decrease training, a preliminary analysis of the data indicated that amount of water added to the stomach was consistently correlated with acid secretion across subjects. These correlations suggested that changes in acid secretion might have been produced by varying the distension of the stomach with water. To evaluate this possibility, the average amount of water added during the last several days of increase training was computed for Subject C.C., and an equivalent amount of water was added each day of decrease training. This resulted in an average of 3.35 ml/min of water added during the last seven increase training sessions *versus* 3.31 ml/min in the seven decrease sessions. These essentially equal amounts of water added were associated with average rates of acid secretion of 0.0519 mEq/min and 0.0277 mEq/min, respectively. Thus, changes in acid secretion associated with the two contingencies of reinforcement appeared to be independent of amount of water added by the experimenter. (This analysis was based on the middle 75 min of each 105-min session.)

Of the possible mediating variables measured, only amount of water added and gastric motility were positively correlated with acid secretion (0.435 and 0.226 respectively). The multiple correlation of these plus respiration, abdominal EMG, and movements of the electrode was 0.4549. Heart rate correlated -0.065 with acid secretion.

Subject B.S.

The baseline average, shown in Figure 6, was 0.0741 mEq/min (range: 0.0642 to 0.0918). There was no apparent tendency for the rate of secretion to increase across baseline sessions. However, during a session in which the effects of colored stimulus lights were being evaluated, a baseline measurement period was introduced, and this was associated with a rate of secretion well above baseline (Section B of Figure 6). This may have been due either to incomplete

habituation or to the residual effects of gastric irritation observed in this subject before this session.

During the first 21 sessions of increase training, depicted in Section C of Figure 6, the DRH contingency was preceded and followed by 15-min timeout periods. For the first few DRH sessions, the rate of secretion was high and quite variable. Gradually, however, rate of secretion declined until the average was lower than the initial baseline. The timeout periods were then eliminated (Sessions 22 to 27), but rate of secretion continued to decline. Thus, for this subject, the DRH schedule did not acquire control over increased acid secretion.

Further analysis of the data suggested that an alternative response might have come under the control of the reinforcement contingencies, namely, rapid gastric emptying. This would produce a high frequency of reinforcement with no increase in acid secretion because a larger change in pH is produced by the same amount of acid secretion when the volume of the stomach contents is reduced.

Support for this possibility comes from an analysis of the amount of sodium bicarbonate

Fig. 6. Subject B.S. A, baseline sessions; B, effects of stimulus lights in one session; C, increase (DRH) training sessions. In Section B, point R is red light, point G is green light, point B is baseline. Data represented in sections A and C do not include first and last 15 min of each session. Ordinate is average rate of sodium bicarbonate infusion required repeatedly to neutralize gastric secretions. See text for details.

required to neutralize gastric pH to 5 once it had fallen to pH 2. The amount of bicarbonate required should decrease as the volume of the stomach contents decreases. In fact, the average amount of bicarbonate required was found to be significantly less ($p < 0.01$) during the last five conditioning sessions (0.190 mEq) compared to the five baseline sessions (0.599 mEq), despite the fact that significantly ($p < 0.01$) more water was added during the last five conditioning sessions. Gastric motility also tended to be greater at the end of conditioning than during baseline, but this difference was not significant.

Discrimination Training

For Subject C.D., an attempt was made to establish stimulus control over differential rates of acid secretion. The procedures used included (a) unsystematic alternation between the DRH and DRO schedules with a distinctive stimulus light associated with each for 12 sessions, (b) systematic alternation between the DRO schedule and timeout periods with a cue light for the DRO schedule during 15 sessions, and (c) systematic alternation between DRH and DRO schedules with distinctive stimulus lights associated with each during 21 sessions. None of these procedures was effective.

DISCUSSION

Results of this investigation indicate that human gastric secretion can be brought under the control of visual feedback that is related to monetary reward. Three of four subjects increased their fasting rate of secretion to three times baseline values when acid secretion was reinforced on a DRH schedule. For all three, acid secretion returned to baseline or below when the reinforcement contingency was changed to DRO. For one subject, rate of secretion did not increase in response to the DRH schedule. It was suggested that an alternative response came under control, namely, rapid emptying of the stomach.

The DRO schedule did not reliably reduce

acid secretion below baseline. This raises the possibility that the DRO contingency may have been ineffective and that decreased secretion may represent extinction. However, data from Subject P.S., showing that an 11-day interruption in the sequence of DRH sessions resulted in no diminution, show that the DRO schedule was more effective than simple lack of exposure to the experimental procedures. The DRO schedule reduced secretion within one to five sessions.

Because the DRO contingency was apparently effective in reducing high rates of secretion in normals, it may prove effective for duodenal ulcer patients, in whom acid secretion is also greater than normal. Analogous differences in the response of hypertensive patients and normals to relaxation training have been reported (Tasto and Shoemaker, 1973). Relaxation training significantly reduced blood pressure in hypertensive patients but not in normals.

Maintenance of learned changes after training is also important to assessing the clinical value of these techniques. Maintenance was not systematically evaluated in this study, although data from one subject suggest that learned increases were maintained for at least 11 days. Animal studies indicate that learned changes in heart rate are maintained for at least three months without intervening practice (DiCara and Miller, 1968).

Differences between subjects in the time required to establish control over acid secretion appeared to be related to the conditioning procedures used. In the first two subjects, acid secretion was reinforced throughout each session, and substantial increases were produced within 10 DRH conditioning sessions. The remaining two subjects were initially tested with 15-min timeouts at the beginning and end of DRH sessions, and no increase in acid secretion was observed within 25 to 27 DRH sessions. When one of these latter subjects was switched to reinforcement throughout the session, her rate of secretion eventually increased. The inference that changing contingencies within a session was responsible for these differences in outcome

is supported by the data for Subject C.D. In this subject, rapid control was established over both increases and decreases when the appropriate contingencies were presented in separate sessions; however, when both contingencies were presented in the same session, control could not be established.

Analysis of the correlation of gastric acid secretion with gastric motility, striate muscle activity, respiratory frequency, amount of water injected into the stomach, and number of times the position of the electrode in the stomach was adjusted revealed substantial correlations in some subjects. However, only amount of water added was consistently and positively correlated with acid secretion across subjects, and a control study in one subject indicated that amount of water added could not account for the observed changes in secretion. Multiple correlation coefficients of all these variables with acid secretion ranged from 0.4274 to 0.5498 in individual subjects. The existence of these high correlations should not be interpreted to mean that the operant contingencies were not governing acid secretion, as is clearly shown by the relationship between procedures and outcomes obtained. It is possible that subjects working for monetary reinforcement bring into play a variety of physiological and other mechanisms that help produce and maintain the response required for the reinforcer to be delivered. Whether there are individual differences in the mechanisms employed, and whether the amount or nature of their contribution changes as consequential control is established, are interesting questions that cannot be answered by these data.

Analysis of the correlations between acid secretion and heart rate (range: -0.065 to 0.444) and between acid secretion and motility (range: -0.010 to 0.226) suggested that the observed changes in acid secretion were relatively specific and could not be attributed to a generalized change in vagal tonus.

Tests of the potential for cognitive mediation proved inconclusive. However, no subject reported using a strategy involving cognitive me-

diation. One subject reported that rapid shallow breathing increased acid secretion, but the low correlation between respiratory frequency and acid secretion did not support this hypothesis.

These results are in agreement with the reports of Gorman and Kamiya (1972) and Welgan (1974) in indicating that gastric secretion can be brought under consequential control. These results differ from the reports cited in failing to show control over differential rates of secretion within the same session.

The finding that rate of human gastric acid secretion can be modified with operant-conditioning procedures suggests that such procedures may be useful in the treatment of hypersecretion associated with duodenal ulcer.

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