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Shock predictability and plasma gastrin in the rat

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Rats with chronic gastric cannulas were immobilized in restraint cages and were subjected either to predictable shock, unpredictable shock, or simply restrained. All rats were immobilized only for 4 h. During the second and third hours, rats in the predictable shock and unpredictable shock groups received their respective treatments. Gastric secretion was collected after each hour, and plasma gastrin estimates were obtained after the first and third hours. Shock stress produced a significant inhibition of total acid output for the two shock treatment groups. However, statistically significant plasma gastrin differences were not observed either between treatment groups or between prestress and poststress measures. The data support contemporary clinical observations that gastrin activity is greater in patients with duodenal ulcers, and not significantly different from control values in patients with gastric ulcers.

During the past decade, a number of techniques have been developed for producing gastric ulcers in the rat. Some of these techniques purport to produce lesions by manipulating psychological variables (Ader, 1963; Caul, Buchanan, & Hays, 1972; Moot, Cebulla, & Crabtree, 1970; Weiss, 1970). The extent to which gastric acid is involved in the development of these psychogenically induced lesions is largely unknown. In one procedure, rats subjected to unpredictable shock stress have more stomach ulcers than rats subjected to predictable shock (Sawrey, 1961; Seligman & Meyer, 1970). Restraint plus unpredictable shock produces more ulcers than restraint plus predictable shock (Caul, Buchanan, & Hays, 1972; Mezinskis, Gliner, & Shemberg, 1971; Weiss, 1970). In a previous study (Paré & Livingston, 1973), the present authors observed that restraint plus either predictable or unpredictable shock resulted in a significant decrease in stomach acid secretion as compared to restrained no-shock controls. Since some investigators (Trudeau & McGuigan, 1970) have suggested that an inverse relationship exists between basal gastric acid secretion and serum gastrin levels, the possibility exists that restraint plus unpredictable shock may yield higher gastrin levels as compared to control conditions. This hypothetical relationship may be significant since gastrin represents one of the main mechanisms controlling acid secretion (Brooks, 1970); since gastrin release is subject to a cephalic phase (Grossman, 1966), the manipulation of psychological stress variables may have some input into the stimulation of gastrin release. The existence of a relationship between serum gastrin and psychologenically induced stomach lesions would also support Dragstedt's (1965) position that gastrin plays a major role in the development of gastric ulcers. The purpose of the present study was to measure gastrin levels in rats subjected to an experimental technique, which in the past has been shown to have ulcerogenic effects.

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MATERIALS AND METHOD

Eighteen male Sprague-Dawley rats (270-293 g) served as subjects. The immobilization apparatus consisted of plastic restraining cages (Scientific Products) measuring 17.8 cm long and 8.2 cm wide on the inside. A slot was cut out of the cage floor to accept a gastric collection tube. The rat's tail also protruded through the rear of the cage and was available for blood collection purposes. The restraint cages were individually housed in sound-attenuating enclosures. Shock was provided by a Grason-Stadler Model E1064GS shocker. Electromechanical programming equipment controlled the sequence and presentation of tone and shock events.

Chronic gastric cannulas were surgically implanted in all 18 rats. The cannula and surgical procedure are described in detail in an earlier report (Paré, 1972). Following an 18-day postoperative recovery period, rats were placed in restraining cages on successive days for 15, 30, 60, 120, 240, 360, and 480 min, respectively. This procedure was followed simply to gradually habituate the rats to the restraining cages. Following this habituation period rats were food deprived for 19 h. The screw plug from the cannula was then removed and the stomach was lavaged and drained through the cannula with 5-10 ml of warm saline until the effluent was clear. The gastric juice collection tube was then screwed into the cannula and the rat was placed in one of the restraining cages and remained therein for 4.5 h. For the first 30 min gastric juice was drained and not collected. A plastic vial was subsequently connected to the collection tube and 1-h gastric samples were collected for the next 4 h. The first and fourth hours were shock-free periods and were considered rest periods. During the second and third hours, shock electrodes were taped to the rat's tail and the animals were presented with tone and shock presentations; this period was considered the stress period. Rats were divided into three treatment groups: predictable shock, unpredictable shock, and no-shock control. Predictable-shock rats (n = 6) received a 10-sec, 84-dB tone (re .0002 dyne/cm^2) followed by a 2-sec, 1.5-mA tail shock. The time interval between tone-shock pairings was random but averaged 60 sec. Unpredictable-shock rats (n = 6) received the same number of tones and shocks, but tones occurred randomly with no relationship to the scheduling of the shocks. Control rats (n = 6) received tones, but no shocks. A tail-blood sample (0.5-1.0 cc) was obtained from each rat at the beginning of the first and fourth hours and represented pre- and

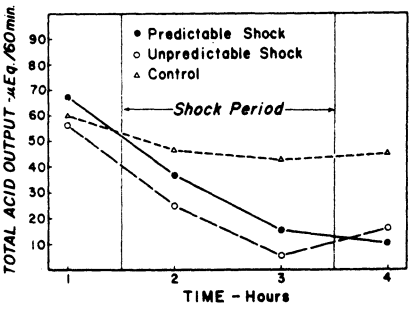

Figure 1. Mean total acid output for the three treatment groups.

poststress samples. From each plasma sample two 100 microliter quantities were utilized to perform duplicate gastrin analyses on each plasma sample. Plasma gastrin estimates were obtained by a radioimmunoassay technique using a Squibb (Princeton, New Jersey) gastrin immutope procedure. Hourly gastric samples were measured for volume and total acid output. The concentration of the hydrogen ions was determined electrometrically with a pH meter by titrating 1-ml samples with .01 N NaOH to a pH of 7.0. The total acid output was obtained by multiplying the volume of the sample by the hydrogen ion concentration. Differences between group plasma gastrin values as well as pre vs. poststress values were analyzed using an analysis of covariance design (Ostle, 1958). Total acid output values were evaluated by an analysis of variance design for repeated measures (Winer, 1962).

RESULTS

Total acid output values are illustrated by Figure 1. Analysis of variance of these data revealed a statistically significant difference for the various hourly collection periods ($F = 11.55$, $df = 3,45$, $p < .01$). Comparison of group means indicated that differences between collection periods were attributable to the significantly lower total acid output values for the predictable and unpredictable shock groups as compared to the control group values for second stress hour and the poststress hour (Tukey a test, $p < 0.05$). Total acid output values for the control group were not significantly different for the four collection periods. A differential group effect failed to materialize for the plasma gastrin values (see Table 1). Differences between treatment group gastrin means were not significantly different for the prestress period ($F = 0.30$) nor for the poststress period ($F = 0.10$). Although gastrin levels were higher for the poststress period, these were not significantly different from prestress values ($F = 0.09$).

Table 1
Mean Prestress and Poststress Plasma Gastrin Values (pg/ml) for the Three Treatment Conditions

Treatment Conditions	Prestress Mean	Prestress SE	Poststress Mean	Poststress SE
Unpredictable Shock	34.20	7.64	50.00	7.21
Predictable Shock	38.58	11.46	45.83	10.25
No-Shock Control	41.60	12.64	47.05	11.49

DISCUSSION

The present data illustrate that acute stress produces an inhibition of gastric secretion. As such, these data replicate earlier observations from this laboratory (Paré & Livingston, 1973; Paré & Isom, 1975). The gastrin results would suggest that gastrin is not related to gastric ulceration produced by unpredictable shock. These results are in accord with reports indicating that gastrin activity is higher in patients with duodenal ulcers but not significantly elevated in patients with gastric ulcers (Brynes, Young, Chisholm, & Lazarus, 1970; Emas, Borg, & Fyro, 1971; Giles & Clark, 1967; Herring & Blair, 1969; Walsh & Grossman, 1973). Goebbels and Adkins (1967) have demonstrated that subcutaneous injections of gastrin result in duodenal ulcers in the guinea pig, and Emas and Grossman (1967) produced duodenal ulcers in the cat by infusing gastrin. In neither of these studies did exogenous gastrin produce significant gastric ulceration. Since gastrin levels for shock groups in the present study were not different from those of control animals, the suggestion must be considered that gastrin is not involved in lesions produced by this ulcer model. Of course, the possibility must be considered that the unpredictable shock ulcer model is not a very efficient ulcer-producing technique and consequently not the optimal research technique for demonstrating possible gastrin responses to psychogenic variables.

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