Hypophysectomy promotes gastric lesions in rats

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Much research suggests that hypophysectomy renders an animal especially vulnerable to the effects of stress. In this experiment hypophysectomized rats were found to be much more susceptible to restraint-produced gastric lesions than were sham-operated controls (4.5 vs. 0 mean lesions). Concurrent behavioral measures of nociception did not distinguish between the two groups.

It has been reported that hypophysectomy has no effect on the formation of restraint-produced gastric lesions (Brodie & Hanson, 1960; Hanson, 1963; Menguy, 1960). These results are surprising, considering the importance of the pituitary gland in the general adaptation syndrome (Selye, 1946, 1976). One would suspect that removal of the hypophysis would render an animal especially vulnerable to the effects of stress and that this vulnerability would be reflected in greater susceptibility to stress ulcers (cf. Selye, 1950, p. 697). Related research has focused on sensory and perceptual changes resulting from hypophysectomy. Hypophysectomy attenuates stress-induced analgesia resulting from immobilization (Amir & Amit, 1979), cold water swim (Bodnar, Glusman, Brutus, Spiaggia, & Kelly, 1979), insulin injections (Bodnar, Kelly, Mansour, & Glusman, 1979), and intermittent footshock (Terman, Shavit, Lewis, Cannon, & Liebeskind, 1984). Research on whether hypophysectomy affects nociception to electric shock has had mixed results. Gispén and colleagues (Gispén, van der Poel, & van Wimersma Greidanus, 1973; Gispén, van Wimersma Greidanus, & De Wied, 1970) have noted greater sensitivity in hypophysectomized rats to electric shock while others have observed no significant effects (Gibbs, Sechzer, Smith, Connors, & Weiss, 1973; Rodgers & Semple, 1978). This is an important issue because differential ulceration in hypophysectomized animals could be attributed to lowered pain thresholds, which result in greater stress. The purpose of this experiment was to examine the effects of hypophysectomy on ulcer formation in the rat while concomitantly taking behavioral indices of nociception.

METHOD

Subjects

The animals were 16 male Long-Evans rats (about 10 weeks old) from Blue Spruce Farms (Altamont, NY) with a mean body weight

of 255.5 g. They were housed individually in a room with a 12-h/12-h light/dark cycle (lights on at 07:00). The rats were maintained ad lib on water, Wayne Lab-Blox, and 10% dextrose solution; however, all subjects were deprived of dry food 48 h prior to the start of the ulcer induction procedure. The animals did not receive any hormone replacement therapy.

Apparatus and Procedure

The rats were equally and randomly divided into hypophysectomized (hypox) and sham-operated groups. Under ether anesthesia, the hypophysis was removed by aspiration via the transauricular approach (Falconi & Rossi, 1964). The hypophysis was reconstructed in a Petri dish at the time of the operation. Animals were given 10 to 14 days to recover. The rats were placed in Plexiglas restraint tubes that were 14 cm long and had an inside diameter of 5.08 cm (for greater details and a drawing of the restraint tubes see Guile & McCutcheon, 1980). The rats were run with normal room illumination (fluorescent lights). After being restrained, but prior to attachment of tail electrodes, the two groups were tested for tailflick latencies (to the nearest 0.1 sec) to a radiant heat source. Pilot research with this procedure had demonstrated a mean $\pm$ SE tailflick latency of 9.3 sec $\pm$ 0.5 in nonoperated animals. During the 6 h of restraint, all rats were tested hourly for flinch and vocalization levels (in mA) to electric shock delivered through tail electrodes. An ascending series method was used, starting at 0 mA and increasing in 0.25-mA steps approximately every 20 to 25 sec until the response occurred at two successive steps. The flinch and vocalization points for the trial were defined as the shock values that elicited the first response. These shocks were unsignaled. This behavioral measure of nociception has been used to measure signaled shock antinociception (Guile & McCutcheon, 1984) and brain stimulation analgesia (McCutcheon & Guile, 1980, 1984). At the end of 6 h a terminal blood sample was obtained by cardiac puncture with a heparinized syringe. Blood samples were immediately centrifuged for 22 min at 24,000 rpm. The plasma was then stored at -20° C until assayed (Bartke, Steel, Musto, & Caldwell, 1973) for testosterone. The stomachs were promptly removed and scored for number and cumulative length (in millimeters) of glandular stomach lesions. As an additional check on completeness of the hypophysectomies, seminal vesicles and testes were removed, blotted dry, and weighed to the nearest 1 mg. Two-tailed Mann-Whitney U tests were performed on ulcer scores and tailflick latencies. Analyses of variance were performed on the flinch and vocalization data.

RESULTS

The results are presented in Table 1. There was no overlap between the lesion scores of the groups ($U_s = 0$, $p < .001$) and no significant difference with regard to tailflick latencies ($U = 25$, $p > .2$). Neither main effects nor interaction of hypophysectomy and repeated

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Table 1
Means and Standard Errors for Sham-Operated (Sham)
and Hypophysectomized (Hypox) Groups

Dependent Variable	Sham Group	Hypox Group
Lesion count*	0 ± 0	4.5 ± 1.4
Cumulative lesion length*	0 mm ± 0	1.8 mm ± 0.6
Tailflick latency	9.8 sec ± 1	10.8 sec ± 0.8
Flinch level	0.24 mA ± 0.02	0.25 mA ± 0
Vocalization level	0.27 mA ± 0.03	0.28 mA ± 0.4
Plasma testosterone*†	1.35 ng/ml ± 1	0 ng/ml ± 0
Seminal vesicle weight*	251 mg ± 10.6	67 mg ± 8.3
Testes weight*	3.065 g ± 0.07	1.646 g ± 0.13

*No overlap in scores between the groups. †Sensitivity is 10 pg.

measures were significant in the analyses of the flinch and vocalization nociceptive measures. Consequently, the results are collapsed into a single mean for each measure and group. The measurements reflecting completeness of the hypophysectomies (plasma testosterone, seminal vesicle weight, and testes weight) showed no overlaps between the hypophysectomized and the sham-operated rats.

DISCUSSION

Hypophysectomized rats were more vulnerable to restraint-induced gastric lesions than were sham controls. There were no significant differences between the two groups in nociception. The differences in plasma testosterone, seminal vesicle weight, and testes weight were consistent with complete hypophysectomies. The present gastric lesion results are in contrast to previous experiments, which found negative results (Brodie & Hanson, 1960; Menguy, 1960). The reasons for the difference in results are open to speculation. There are a myriad of differences between the present and previous studies, including the mode of restraint. Both Brodie and Hanson (1960) and Menguy (1960) literally wrapped their rats in wire mesh, affording them a much tighter fit (and corresponding greater degree of restraint) than was used in the present study (cf. Guile & McCutcheon, 1980). This may account for the difference in results. For instance, 100% of Menguy's rats ulcerated in both the hypophysectomized group and the control group, suggesting a "ceiling effect." The rats in both groups may have been restrained so severely that it overwhelmed any hormonal differences between them.

The lack of differences in the measures of nociception between sham-operated and hypophysectomized animals corroborates similar findings elsewhere (Gibbs et al., 1973; Rodgers & Semple, 1978). However, the interpretation of null results is problematical, particularly because research has demonstrated inconsistencies between tests for measuring analgesia (Brase, 1979; Kordower, Simone, Merrigan, & Bodnar, 1981; Stern & Kelly, 1981). One could ask the question, did both groups show analgesia, or did both fail to show analgesia? I would argue that the latter alternative is correct, inasmuch as the responses of the two groups remained at the lowest current settings over the course of the 6-h session. These results suggest that

the large differences in ulcer scores are not due to differential pain thresholds between the two groups, which would affect their perception of the aversiveness of restraint (cf. Guile & McCutcheon, 1984, for differences in ulcer scores concomitant with changes in nociception scores). Given these findings, it would be appropriate to examine hypophysectomy's direct effects on the stomach (e.g., Kyle, Clarke, Ward, Adesola, & Welbourn, 1963; Robert, Phillips, & Nezamis, 1966; Schapiro, Wruble, & Britt, 1970; Taché, Goto, Gunion, Rivier, & Debas, 1984) in the context of the present study.

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