

Scientific work conducted at Peter I Island on 28 and 29 February and 1 March showed that the island covers less area and is higher (about 5700 feet rather than 4005 feet) than shown on U.S. Navy hydrographic chart HO-6630. Peter I Island is an extinct, deeply dissected volcano, almost entirely capped by ice; most rock is exposed on steep cliffs. At Norwegia Bay on the west side of Peter I Island, gray to dusky red, dense to vesicular basalt flows and bedded tuffs are cross-cut by basic dikes and a hypabyssal plug. The basaltic rocks contain olivine phenocrysts and mafic to intermediate inclusions (5).

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Distinct "Feeding" and "Hunger Motivating" Systems in the Lateral Hypothalamus of the Rat

Abstract. Electrodes were implanted in the middle hypothalamus of rats to determine the neural organization of the "feeding" centers. Stimulations of the far- and midlateral hypothalamic area produced feeding responses in sated animals, but only the former caused sated animals to cross an electrified grill to press a lever for food. After lesions had been made in the medial forebrain bundle, however, stimulations in the far-lateral hypothalamic area resulted in feeding in sated animals but failure to cross the electrical barrier to press a lever for food. Simultaneous far-lateral and "satiety" center stimulations produced feeding in sated animals but failed to "motivate" grill-crossing behavior.

The middle hypothalamus functions to regulate food intake in several animal species and has been shown to be organized into a lateral "feeding" center and a medial "satiety" center (1). Anand and Dua (2) presented evidence that the lateral "feeding" center maintains constant facilitatory influences on feeding behavior and is held in check by the more medial "satiety" region, which presumably generates inhibitory impulses in response to monitoring

some circulating material indicative of the satiated state. Previous evidence (3) shows that the medial forebrain bundle, for which the lateral hypothalamus serves as a bed nucleus, is not the critical lateral hypothalamic system controlling basic feeding behavior, since lesions in this bundle anterior or posterior to the level of the ventromedial nuclei do not alter feeding behavior in the rat. Aphagia and adipsia result only with lesions in this bundle at the ventromedial level. Morrison, Barnett, and Mayer (4) have claimed that "the medial forebrain bundle itself may be as important as the lateral hypothalamus in the control of feeding behavior," but they failed to take into account that many other systems cross the lateral hypothalamus at the level of the ventromedial nuclei. Furthermore, the lesioning method in the complexly organized lateral hypothalamus cannot possibly dissociate the medial forebrain bundle fibers from the several other trajectories, mostly pallidofugal, which enter the hypothalamus at this level. The present experiments were undertaken to fractionate functional components comprising the "feeding" center so as to ascertain the relative importance of the several systems comprising the "center" and, more particularly, to determine the possible means by which an interplay occurs between the "feeding" and "satiety" areas.

Numerous studies on feeding behavior have used a single measurement—that is, the amount of food consumed—as a determinant of "appetite," whereas in reality the essential "hunger" drive is best determined by the effort an animal will go to in order to overcome a barrier to obtain food. That certain specific "motivational" systems exist in the lateral hypothalamic area of the rat has been shown by Olds (5), who has found that the more general motivating properties of hunger may be produced by electrical stimulation of specific points in the brain, especially along components of the medial forebrain bundle. Since our previous studies indicate nonessentiality of this bundle in basic feeding reactions, it may well be that the medial forebrain bundle is at least important in motivating barrier crossing to obtain food, that is, as a system concerned with "hunger." Thus an attempt to study this system and its relationships with the feeding facilitatory mechanisms lying in the far-lateral portion of the middle hypothalamus comprise a part of the present study.

Adult male and female albino rats were tested for several days in a Skinner box for lever-pressing activity for food under various conditions of

starvation and satiation. After several days of training for several hours a day to establish baseline lever-pressing and feeding behavior, bipolar electrodes were stereotaxically implanted in the far-lateral hypothalamic area in four animals and in the midlateral hypothalamic area in three animals. Four additional animals were given bilateral lesions in the medial forebrain bundles; then, after a testing period, electrodes were implanted in the far-lateral hypothalamic area. Three other animals had electrodes implanted in the medial forebrain bundle anterior and posterior to the level of the "feeding" centers. Finally three animals had electrodes implanted simultaneously in the far-lateral hypothalamic area and "satiety" regions. Postoperatively, after readjustment to the testing box and lever-pressing routines were set up, continuous 10-minute stimulations were carried out 20 minutes apart for 3 hours (total of six 10-minute stimulations). The stimulus parameters used were square-wave pulses of 0.2-msec duration, 60 cy/sec, at 1 to 3 volts.

Electrical stimulation of the far-lateral hypothalamic area consistently resulted in high lever-pressing rates for food and voracious feeding in satiated animals as well as "motivation" to cross an electrified grill to lever-press and feed. Stimulations in the midlateral hypothalamic area, although they often produced feeding in satiated animals, never resulted in running of the electrified "barriers" to lever-press for food. Animals with lesions in the medial forebrain bundles anterior and posterior to the level of the "feeding" centers showed no disturbances in feeding behavior. They would not feed in the sated state and never ran the electrified grill. However, after these lesions, stimulations in the far-lateral hypothalamic area still produced feeding in sated animals but no "motivation" to cross the electrical barrier to lever-press for food. Stimulations in the medial forebrain bundle itself anterior or posterior to the level of the "feeding" centers resulted neither in feeding behavior or barrier-crossing in sated animals. Simultaneous stimulations in the far-lateral hypothalamic area and "satiety" centers resulted in feeding in sated animals but consistent failure to run the electrical barrier to lever-press for food.

These data seem to indicate that the medial forebrain bundle is important in the organization of the "feeding" center as a "hunger motivational" system, since overcoming "barriers" to get to food (a measure of "hunger") depends on the essential integrity of this bundle. With this bundle interrupted, no "hunger motivation" seems to be present in

sated animals after far-lateral hypothalamic stimulation, although pure feeding responses are obtained. Thus basic feeding responses occur without the bundle but the animal will not "work" for its food. Since stimulation of the feeding and satiety areas simultaneously produces feeding in sated animals but not grill-running to lever-press for food, it seems likely that the "satiety brake" is acting on the medial forebrain bundle "motivational system" and not on the far-lateral hypothalamic basic feeding mechanisms. These results probably indicate the presence of motivational elements in the medial forebrain bundle necessary for "hunger drive" which are selectively suppressed by the "satiety" center. The far-lateral hypothalamic area would thus seem to contain the basic elements concerned directly with activation of specific feeding reflexes. It is concluded, therefore, that the "feeding" center probably is composed of both basic "feeding" and "hunger drive" elements, only the latter being depressed by the satiety mechanism (6).

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Radioprotection by Mitotic Inhibitors and Mercaptoethylamine

Abstract. In the mouse, chemical interference with cellular proliferation alters the radiosensitivity of the bone marrow, and this results in protection from otherwise lethal x-irradiation. When intestinal damage is minimized by appropriate timing and dosage, many mitotic inhibitors increase radioresistance and enhance the protective effects of mercaptoethylamine.

It has been postulated that radioprotective chemicals operate by way of tissue hypoxia, inactivation of free radicals, or by the formation of mixed disulfides, or by all three (1). However, such mechanisms fail to explain the delayed protection against lethal

Table 1. Survival data of mice receiving single large doses of mitotic inhibitors, alone and combined with mercaptoethylamine. Individual results represent groups of ten treated and ten control animals exposed to lethal x-irradiation.

Inhibitor	Intraperitoneal administration prior to x-ray		800 r 30-day survival (%)	
	Dose (mg/kg)	Time (hr)	Agent alone	Agent plus MEA*
<i>Metaphase inhibitors</i>				
Colcemide	50	1	50	100
Colcemide	50	12	0	30
Colcemide	50	48	20	100
Sodium arsenite	12.5	24	40	100
Cadmium chloride	2.5	24	10	70
<i>Preprophase inhibitors</i>				
Epinephrine	2	24	10	80
Urethan	1000	48	50	90
Cortisone	200	48	10	30
T-P vaccine†	†	24	10	100
<i>Mercaptoethylamine</i>				
MEA	75	0.25	30	

* Mercaptoethylamine, 75 mg/kg, 15 minutes before x-ray. † Typhoid-paratyphoid vaccine (Pitman-Moore), 0.5 ml per mouse.

radiation reported by Smith (2) for a colchicine derivative, or by Cole (3) for urethan. These latter agents have at least one common feature. That is, correct dosage results in mitotic inhibition followed by changes in cellular proliferation (4). With this feature as a working hypothesis, we have studied the effect of a series of mitotic inhibitors upon the radiosensitivity of mice. Preliminary results allow us to describe the action of a large class of radioprotective agents both singly and when combined with mercaptoethylamine, a known radioprotective compound.

Young female mice (Bagg Swiss), weighing 20 to 25 g, were used. Equal numbers of control mice were irradiated simultaneously with each treated group and thereafter housed jointly. Irradiations were accomplished with a G.E. Maxitron unit: 300 kv; 20 ma; HVL, 2 mm Cu; TSD, 85 cm; dose rate, 45 r/min. The 800-r dose of x-irradiation was uniformly lethal in these experiments, all control mice dying before the 21st day after exposure.

The survival data in Table 1 show clearly that mitotic inhibitors are capable of decreasing the sensitivity of mice to lethal x-irradiation. Likewise, pretreatment with these agents enhances the radioprotective effect of a small dose of mercaptoethylamine. The cytotoxic action of the mitotic inhibitors has been documented adequately by Bieseke (4).

Most mitotic inhibitors depress both the hematopoietic tissue and the gastrointestinal epithelium, but the time for maximum depression varies for each tissue. This variation allows one to achieve selective inhibition by proper timing and optimal drug dosage. It be-

came evident early in the course of our studies that we must avoid a combination of chemical and radio-inhibition of the intestinal epithelium. Either injury causes some degree of cell depletion and tends to increase radiosensitivity. Combined inhibition leads to severe intestinal damage which is expressed clinically by diarrhea and death 5 to 8 days after 800 r of x-irradiation (5). The results obtained with colcemide (6) (Table 1) demonstrate a biphasic effect upon radioresistance, with loss of protection 12 hours after administration of the drug. This time-effect fits the response curve for colchicine-induced inhibition of the gut as reported by Friedman (7).

Our experiments suggest that proper timing in the use of mitotic inhibitors will permit selective alteration of the radiosensitivity of the bone marrow. This alteration is manifested by an increase in radioresistance, and by a greater response to the protective effects of mercaptoethylamine, as measured by 30-day lethality.

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