whose lymphocyte counts are markedly elevated (12,13). Schrek concluded that CLL lymphocytes are heterogeneous with respect to PHA responsiveness and that "low count" CLL is associated with a greater percentage of PHA responsive cells. However, the present data suggest that even in "low count" CLL, the PHA-responsive lymphocytes were not normal as the development of maximal rates of nucleic acid synthesis was still delayed. This delayed response to PHA may represent a primary proliferative abnormality of CLL lymphocytes evident during the early phases of the disease. Progression of the disease, as manifested by increasing lymphocytosis might be accompanied by total loss of reactivity.

Summary. The kinetics of RNA, DNA, and protein synthesis were analyzed in normal and CLL lymphocytes stimulated by PHA *in vitro*. Normal cultures exhibited maximal increases in lymphocyte nucleic acid and protein synthesis 2 to 3 days after exposure to PHA. Under identical conditions the maximal response on the part of the lymphocytes in CLL cultures occurred between 5 to 7 days. The data suggest that many CLL lymphocytes are capable of responding to PHA but the response is distinctly delayed.

TABLE I. Percentage Blast Cells ± 1 SD in Unstimulated and PHA-Stimulated Cultures from 5 Normals and 5 Patients with CLL after 3 and 7 Days of Incubation.

		3 days	7 days
normal (5)	unstimulated	0.6 ± 0.5	3.1 ± 0.6
	PHA stimulated	63.5 ± 4.2	75.2 ± 6.1
CLL (5)	unstimulated	0.8 ± 0.6	1.1 ± 0.8
	PHA stimulated	10.8 ± 4.2	26.0 ± 5.4

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Effect of Amygdaloid Lesions on Plasma and Pituitary Thyrotropin Levels in the Deermouse*† (32770)

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The importance of the hypothalamus in the modulation of hypophyseal secretion is well documented. In recent years, however, increasing evidence indicates that other areas of the brain may be involved. Specifically, the amygdala, a part of the rhinencephalic-limbic system, has been implicated in the regulation of gonadotropic and corticotropic activity (1–5). More recently, it was found that another hypophyseal hormone, thyrotropin, is not affected by destruction of the amygdala (6–7).

However, since the latter two studies did not indicate which area of the amygdala was involved, and since the amygdala is composed of several nuclear groups, it was decided to repeat these works.

The present work deals with the effects of

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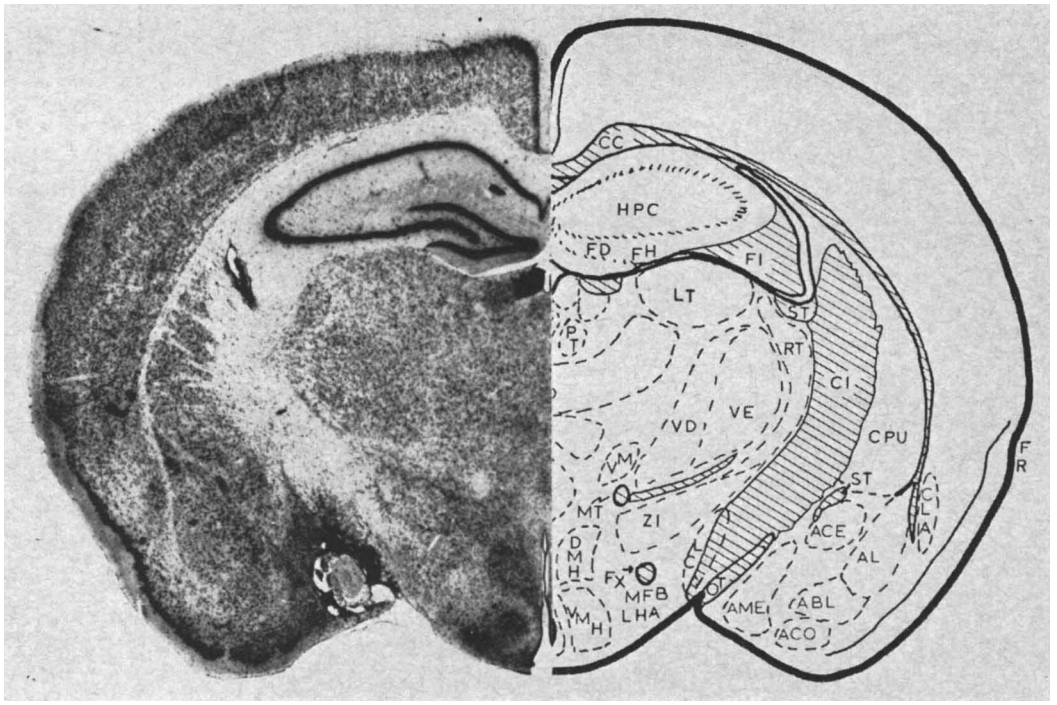

FIG. 1. Diagrammatic and photomicrographic representation of the diencephalon of *P. m. bairdii* with location of lesions. Right hemisphere represents location of various nuclei: ABL = basolateral amygdaloid nucleus; AME = medial amygdaloid nucleus; ACE = central amygdaloid nucleus; ACO = cortical amygdaloid nucleus; AL = lateral amygdaloid nucleus.

lesions in the medial amygdaloid nuclear group on pituitary and plasma levels of thyrotropin in the male deermouse (*Peromyscus maniculatus bairdii*).

Materials and Methods. Adult male deermice *(Peromyscus maniculatus bairdii),* weighing 15–19 gm each, were lesioned in the medial group of the amygdaloid complex according to the stereotaxic atlas for this species, and as in previous studies (8–10).

Three groups of 10 animals each were sacrificed at 3, 8, and 16 days after lesions were made as were 3 groups of 10 animals/group of nonlesioned controls. Furthermore, 3 groups of 10 animals/group were sham operated by inserting the needle in the amygdala but without administering any current. The last animals were sacrificed 3 days after the operation. At the time of sacrifice, thyroid and pituitary glands were excised and weighed to the nearest 0.1 mg, and plasma was collected. Pituitaries were frozen in saline and saved for TSH analyses. The position of lesions was confirmed by histological examination (Fig. 1).

Pituitary and plasma thyrotropin content was estimated according to the method devised by Levey (1962). Receptor animals were male rats of the Holtzman strain, 30 days of age. The rats received 0.01% thyroxine in drinking water. After 10 days on thyroxine–water, the rats were injected intravenously, via tail vein, with the pituitary homogenate (1 mg/0.5 ml) or plasma (1 ml/animal). Three rats were each injected for each plasma sample or pituitary homogenate of normal control lesioned and sham-operated *P. m. bairdii.* In addition, 5 rats/group, were each injected with saline, and 1.25, 2.5, and 5.0 mU of standard TSH.[1] Twenty hours after the injection of plasma, pituitary homogenate, and standard TSH, all rats were injected in-

[1] Special thanks are due Dr. A. L. Caldwell, Jr., of Armour Pharmaceutical Laboratories, Kankakee, Illinois, for the supply of standard bovine TSH sample, Lot No. 216-178-1, used.

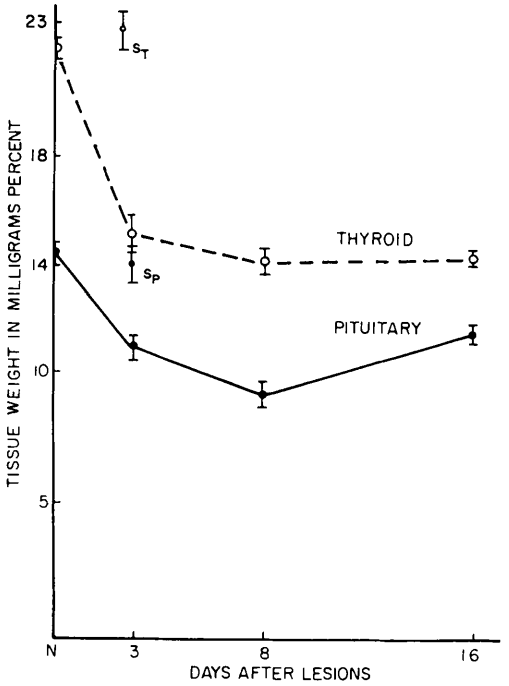

FIG. 2. Weight of pituitary and thyroid glands (in mg/100 gm of body wt) in normal, without lesions, male *P. m. bairdii* and at 3, 8, and 16 days after lesions were placed in the medial amygdaloid complex. Weights of thyroid (S_T) and pituitary (S_P) glands for sham-operated animals also are shown.

traperitoneally with 4 μC of ^{131}I. Four hours after the injection of ^{131}I all rats were sacrificed, thyroids were removed, weighed to the nearest 0.1 mg, and radioactivity was estimated in a well-type scintillation counter. Extrapolation for equivalent mU of TSH of the unknown pituitary homogenates and plasma samples was based on the equation: $Y = 1816 + 1355 \log X$, where Y is the cpm/mg of radioactivity of thyroids of assay rats and X is the mU of TSH. The overall lambda of precision for this assay was 0.2046.

Results. After lesions were placed in the medial amygdaloid group (Fig. 1), weight of the thyroid gland declined significantly ($p < .01$) from a normal, control value of 22.37 to 15.22 mg% at 3 days (Fig. 2). There was a further minor decline to 14.12 mg% at 8–16 days after lesions were made.

The pituitary weight also declined, but not significantly, from a normal 14.42 to 10.98 mg% at 3 days (Fig. 2). Further decline, significant at $< .01$, was noted at 8 days after lesions, when the pituitary reached 9.07 mg%. However, after that decrease in weight, the pituitary weight increased to 11.49% at 16 days after lesions were placed in the medial amygdaloid complex.

The pituitary TSH content of animals with lesions exhibited a significant ($p < 0.1$) rise from an unlesioned, control value of 9.1 to 22.9 mU/mg at 3 days (Fig. 3). That was followed by a moderate decline to 17.1 mU/mg at 8 days, which was significantly ($p < .01$) higher than TSH of *bairdii* without lesions. At 16 days after lesions, the pituitary TSH content was 14.0 mU/mg, still a significantly ($p < .01$) 42% higher than unlesioned controls. Animals sham operated exhibited no significant changes in any of the measurements made.

Plasma levels of thyrotropin declined significantly from a mean of 14.8 mU/ml in *bairdii* without lesions to 8.1 mU/ml at 3 days after lesions were placed in the medial amyg-

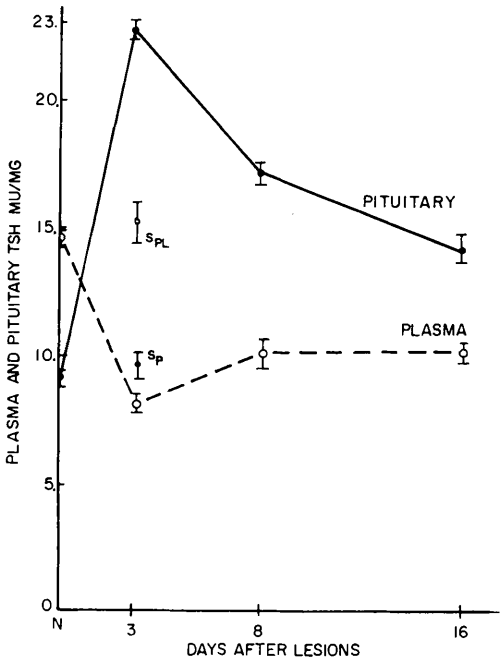

FIG. 3. Pituitary and plasma levels of thyrotropin (in mU/mg or mU/ml) in normal, unlesioned male *P. m. bairdii*, and at 3, 8, and 16 days after lesions were placed in the medial amygdaloid complex (±SE). Plasma (S_{PL}) and pituitary (S_P) levels of TSH for sham-operated animals also are indicated.

daloid complex. That was followed by a 27% increase to 10.3 mU/ml at 8 days, which was significantly ($p<0.01$) lower than controls. Levels of thyrotropin at 16 and 8 days after lesions were identical.

Discussion. The significant increase in pituitary thyrotropin content accompanied by a decline in the circulating level of TSH correlates with the finding that, after lesions, thyroid gland weight declines significantly.

That weight of the pituitary gland declines after lesions is somewhat surprising as one would expect it to increase. The decrease may be explained by the finding that after lesions in the medial amygdaloid complex, circulating ACTH and LH significantly increase in this species (9, 10). Thus the increase in pituitary TSH may be counterbalanced by a decrease in ACTH and LH, so the anticipated increase in pituitary weight is cancelled.

Although additional work is necessary to establish whether the amygdala may modulate pituitary TSH, some tentative assumptions may be made. The present data indicate that lesions in the medial amygdaloid nuclear group affect changes in the release of TSH from the pituitary, which, however, may not be permanent since there is a gradual return to almost normal levels of circulating TSH by day 16.

The finding that the present data are not in complete accord with previous work (6,7) is not surprising, considering that previous work did not indicate the specific area of the amygdala in which lesions were placed. Our findings are based on lesions produced in the medial amygdaloid nuclear group. However, the additional possibility exists that the difference in our work and in previous work may be a matter of species specificity and the consideration cannot be overlooked that the deermouse may be different than the rat.

Further work is necessary to clarify the possible role of the medial amygdaloid complex on pituitary thyrotropin. Results reported here indicate a possible existence of a separate stimulatory center to modulate the pituitary–thyroid axis. The possibility exists that injury from lesions produces a focal point of irritation that may spread to other areas of the brain, mainly to the hypothalamus (12). In our opinion, however, it seems unlikely that such injury would produce sustained irritation of 16 days.

Results of our sham-operated animals agree with similar findings regarding ACTH and LH (9,10,13).

Summary. Bilateral lesions produced by electrocoagulation in the medial amygdaloid nuclear complex were found to affect pituitary and plasma levels of thyrotropin in the male deermouse *(Peromyscus maniculatus bairdii)*. Within 3 days after lesions were placed in the medial amygdaloid complex, the pituitary thyrotropin exhibited a significant rise to 22.9 mU/mg from 9.1 mU/mg in intact, control animals while the plasma level in animals with lesions dropped significantly to 8.1 mU/mg from 14.8 mU/mg in control animals. The rise in pituitary and fall in plasma levels of thyrotropin remained at a significant level, compared with control animals, throughout the 16 days of the experiment, although by day 16 there was evidence of a return to normal for this species. The changes in thyrotropin were accompanied by significant decline in thyroid gland weight throughout the experiment.

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