too alkaline or acid to support respiration. In all experiments the tissue was suspended in a phosphate medium buffered at pH 7.4 with lactate as a substrate. The tissues were inserted in the Warburg respirometer and one-half hour elapsed, the time required for equilibration, before observations were begun.

The data disclose that the O_2 consumption of the brain tissue treated with cysteine exhibits a diphasic response. During the first 30 to 45 minutes there is a marked stimulation which is followed by a profound depression in the later periods. Cysteine, moreover, retains an early stimulatory effect on O_2 consumption despite the presence of cyanide.

In order to obtain further information as to the character of the increased O_2 consumption, a group of observations was made on the R.Q. after the addition of cysteine hydrochloride in a concentration of 0.01 M. In most instances the R.Q. of unwashed, minced brain tissue is approximately 0.9, (Himwich, Fazekas, Barker, Hurlburt[2]) and in these studies the addition of cysteine resulted in a depression of the quotient. In 8 experiments they were found to be 0.50, 0.65, 0.65, 0.54, 0.59, 0.52, 0.30, and 0.83. The presence of the sulphydryl group had obviously caused a consumption of O_2 without the simultaneous production of CO_2.

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Relation of Anterior and Posterior Lobe of the Hypophysis to Insulin Sensitivity in the Rat.*

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The discovery of Houssay and Magenta,[1] since repeatedly confirmed by other investigators, that the hypophysectomized animal becomes extremely sensitive to insulin, led to attempts to determine what part of the pituitary body was involved. The observation

2 Himwich, H. E., Fazekas, J. F., Barker, S. B., Hurlburt, M. H., *Am. J. Physiol.*, 1934, **110**, 348.

* Aided by the Presnell Fund for the study of the metabolic relations of the anterior hypophysis contributed by Robert R. Presnell, Frank Tuttle, Arthur Stebbins and Mrs. Gordon Kahn of Los Angeles.

1 Houssay, B. A., and Magenta, M. A., *Rev. Assn. Med. Argentina*, 1924, **37**, 389; *Comp. Rend. Soc. de Biol.*, 1925, **92**, 822.

of Burn[2] that extracts of the posterior lobe protected normal fasting rabbits against the convulsive action of insulin was confirmed by Geiling, Campbell and Ishikawa[3] in experiments on hypophysectomized dogs. The latter authors also reported that removal of the anterior lobe did not render the dog hypersensitive to insulin, while various operative procedures designed to interfere with posterior lobe secretion had this effect. They concluded that the antagonistic action of the hypophysis to insulin was attributable to the activity of the posterior lobe. Houssay and Potik,[4] on the other hand, found that extirpation of the anterior lobe made toads hypersensitive to insulin and that the daily implantations of one anterior lobe under the skin afforded protection, while similar implantations of posterior lobe had no protective action. This pointed to the removal of the anterior lobe as the cause of the hypersensitivity to insulin.

In connection with anterior lobe removal in the dog it should be pointed out that the anatomical relationships of the canine hypophysis make the complete removal of the anterior lobe extremely difficult, if not impossible, because a portion of the anterior lobe envelopes the dorsal part of the posterior lobe. There is still another factor which has to be considered when the temporal approach is used in the dog as has been done by Geiling and associates, namely, that of brain injury. As shown by Chaikoff, Reichert and collaborators,[5] retraction of the temporal lobe for 2 minutes, so as to expose the pituitary to view but without actually touching it, resulted in hypersensitivity to insulin which persisted in some cases for 3 months.

In view of the conflicting results just enumerated, it seemed desirable to extend this work to an animal form in which the anatomical relationship of the hypophysis is such that it permits the independent removal of either of the two main portions of the hypophysis. Such a condition is offered by the rat. The rat presents another advantage. The sub-diaphragmatic approach to the gland, first described by Smith, makes it possible to remove either lobe unaccompanied by brain injury. It must be admitted, however, that removal of the posterior lobe does involve slight injury to the anterior lobe. Removal of the anterior lobe, on the other hand,

2 Burn, J. H., *J. Physiol.*, 1923, **57**, 318.

3 Geiling, E. M. K., Campbell, D., and Ishikawa, Y., *J. Pharm. Exp. Therap.*, 1927, **31**, 247.

4 Houssay, B. A., and Potik, D., *Comp. Rend. Soc. Biol.*, 1929, **101**, 940.

5 Chaikoff, I. L., Reichert, F. L., Larson, P. S., and Mathes, M. E., *Am. J. Physiol.*, 1935, **112**, 493

can be accomplished without injury to the pars intermedia or pars nervosa. The attachment of the stalk to the brain also remains intact. The histological evidence of the success of such separation will be considered elsewhere.

The experimental material included 164 female rats. Of this total, 105 were completely hypophysectomized; 13 had the posterior lobe and variable portions (in most cases one-half) of the anterior lobe removed; 14 had posterior lobe and a very small fragment of the anterior lobe excised; and 22 had the anterior lobe alone removed. In the last group, the pars nervosa and the intermediate lobe, including their attachment to the brain, were left intact. Brief summaries of the different operative groups are shown in Table I.

TABLE I.

Type of Operation	No. of Animals	Insulin (units/kilo)	No.* Reacting	No. not† Reacting
Complete Hypophysectomy	30	1	25	5
	63	0.5	53	10
	12	0.25	8	4
Incomplete Hypophysectomy‡	13	1	2	11
Anterior lobe only removed§	7	2	7	0
	11	1	11	0
	2	0.5	2	0
	2	0.25	2	0
Posterior lobe removed‖	14	3	1	13

* Convulsion—injected with glucose.
† Spontaneous recovery.
‡ Posterior lobe and approximately one-half of anterior lobe removed.
§ Anterior lobe alone removed. Pars nervosa and pars intermediate intact.
‖ Posterior lobe and a very small fragment of anterior lobe removed.

The hypophysectomized rat is a fragile animal and it seemed inadvisable to secure blood samples by repeated heart punctures. Therefore, in testing its reaction to insulin, the minimum amount of insulin necessary to cause convulsions was used as a measure of insulin sensitivity. Although animals subjected to incomplete hypophysectomy involving the removal of the posterior lobe and one-half or more of the anterior lobe, do show a somewhat greater reaction to small doses of insulin than do normal animals, they are nevertheless much less sensitive than completely hypophysectomized animals. If, however, the operation for removal of the posterior lobe is accompanied by only very slight injury to the anterior lobe, the response of such animals to insulin compares very favorably with that of normal controls. It will be seen that of the 14 animals tested with 3 units of insulin per kilo body weight, only one de-

veloped convulsions; in the remaining 13 animals no disturbance such as tremors or weakness could be detected. On the other hand, the behavior of rats after the anterior lobe only was removed was in no respect different from that shown by the completely hypophysectomized rat. Of the 22 animals tested, 7 succumbed after injection of 2 units per kilo and the intraperitoneal injection of glucose proved of no avail. Eleven of the animals which had received 1 unit of insulin per kilo developed repeated convulsions even after the administration of glucose. The remaining 4 animals, 2 receiving 0.5 units and the other 0.25 units per kilo, also showed convulsions, their death being prevented only by the immediate injection of glucose.

TABLE II.
Blood Sugar After Insulin Injection.*

	Blood sugar in mg. %					
	Initial	0.5 hr.	1 hr.	1.5 hr.	2 hr.	2.5 hr.
Average of 5 normal rats (8-15 hours off food)	113	98	100	111	110	105
Average of 6 rats after removal of anterior lobe (3 weeks post-operative) (8-15 hours off food)	65	34	15	16	15	Died

*0.25 units per kilo were injected intraperitoneally.

Six animals with the anterior lobe removed were anesthetized with amytal and blood was drawn from the jugular vein. The blood sugar values of these animals are shown in Table II. Although the posterior lobe was intact in these animals, the blood sugar dropped to the convulsive level one hour after the injection of only 0.25 units of insulin per kilo. The response of normal animals to a similar dose of insulin is included for comparison. Control experiments, using amytal alone, showed that this anesthetic, *per se,* was not responsible for the blood sugar changes.

Summary. Removal of the posterior lobe of the hypophysis with only slight injury to the anterior lobe does not increase the sensitivity of rats to the convulsive action of insulin. Removal of the anterior lobe only, leaving the posterior lobe intact, results in a marked increase in insulin sensitivity equal to that observed after complete hypophysectomy.