

Insulin Sensitivity of Monkeys after Section of the Hypophyseal Stalk.*

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Disturbances of carbohydrate metabolism including hypersensitivity to insulin have been described in animals following the production of hypothalamic lesions (Ingram and Barris;¹ Cleveland and Davis;² Ingram and Winter;³ Brobeck⁴), and it has been suggested that such disturbances may be due to interruption of nervous connections with the anterior lobe of the hypophysis (Davis, Cleveland and Ingram;⁵ Houssay⁶).

The possibility that the fibers of the hypophyseal stalk are concerned with this function has been disproved by administering insulin intravenously to monkeys (*Macaca mulatta*) which had fully recovered from section of the infundibular stalk just proximal to the dorsal surface of the gland.

The details of operation and exact locations of the lesions have been reported (Magoun and Ranson⁷). The procedure for the tests was the same as that already reported for cats (Brobeck⁴) except that the dosage of insulin used for the monkeys was 0.1 unit per 0.2 kg body weight, and blood samples were taken before insulin injection and afterwards at the end of each hour for 3 hours. Blood sugars were estimated by the Randles and Grigg⁸ modification of the Folin-Wu method.

The results of tests on 3 normal monkeys are compared with tests on 4 operated animals in Graphs I and II. The responses of the 2 groups of animals were quite similar, and the operated animals appeared no more sensitive to insulin than normal. Recovery from hypoglycemia did not take place as rapidly in the monkeys as it does in normal cats (Brobeck⁴), but there was no difference in the amount

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¹ Ingram, W. R., and Barris, R. W., *Am. J. Physiol.*, 1936, **114**, 562.

² Cleveland, D., and Davis, L., *Brain*, 1936, **59**, 459.

³ Ingram, W. R., and Winter, C. A., *Proc. Soc. Exp. Biol. and Med.*, 1939, **41**, 449.

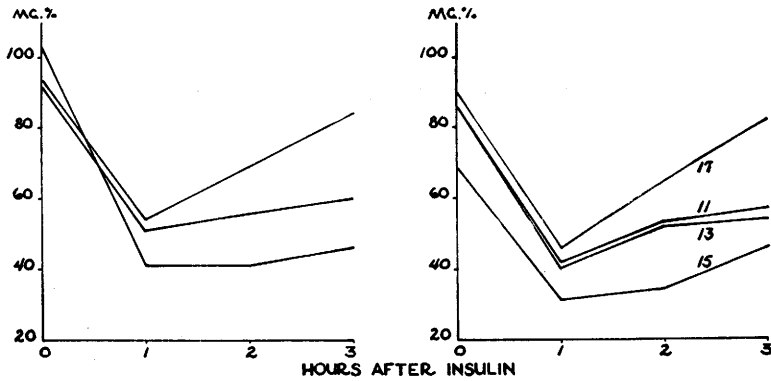
⁴ Brobeck, J. R., *J. Lab. Clin. Med.*, 1939, in press.

⁵ Davis, L., Cleveland, D. A., and Ingram, W. R., *Arch. Neurol. and Psychiat.*, 1935, **33**, 592.

⁶ Houssay, B. A., *New England J. Med.*, 1936, **214**, 971.

⁷ Magoun, H. W., and Ranson, S. W., *Anat. Rec.*, 1939, **75**, 107.

⁸ Randles, F. S., and Grigg, W. K., *J. A. M. A.*, 1924, **82**, 684.



GRAPH 1.
Insulin responses of normal monkeys.

GRAPH 2.
Insulin responses of monkeys 11,
13, 15, and 17, after section of the
hypophyseal stalk.

of recovery shown by normal and operated monkeys, and no external hypoglycemic symptoms were observed.

Fatal hypoglycemia occurred, however, in one insulin experiment not included on either graph; this animal was monkey 16 in which the stalk section was comparable to the others of the series, but in which there was also extensive degeneration of the anterior lobe. The degeneration appeared to be the result of anemic softening and was probably due to interruption of the vessels described by Wislocki and King⁹ in the region of the severed stalk. There was no evidence of hemorrhage and the autopsy revealed no other unusual pathology. Smaller areas of similar degeneration were present in the anterior lobes of 2 of the animals which reacted normally to insulin (monkeys 13 and 15), but the anterior lobes of monkeys 11 and 17 appeared to be intact.

By means of a planimeter, estimations were made of the volumes of normal anterior lobe tissue present after the hypophyses of these animals had been fixed, sectioned, stained and mounted: in monkeys 11 and 17 the glands appeared normal with volumes of 15.3 and 13.5 cu mm respectively; in monkeys 13 and 15 in which small areas of degeneration were present the volumes of normal anterior lobe tissue were respectively 8.8 and 6.2 cu mm; in monkey 16 which died in hypoglycemia the volume of the normal tissue was 4.1 cu mm. The volume of anterior lobe tissue from 4 normal monkeys was respectively 10.9, 14.5, 15.6 and 17.0 cu mm.

Insulin hypersensitivity following hypophysectomy of the monkey

⁹ Wislocki, G. B., and King, L. S., *Am. J. Anat.*, 1936, **58**, 421.

has been reported by Hartman, Firor and Geiling¹⁰ and by Smith, Tyndale, Dotti and Engle¹¹ who also found that partial hypophysectomy did not produce the marked increase in sensitivity which followed complete removal of the gland. The present experiments indicate that insulin responses may be normal when only half of the anterior lobe is left intact.

Infundibular connections between the hypothalamus and pars distalis, however, are not essential for normal insulin sensitivity in the monkey, and are therefore probably not essential for normal carbohydrate metabolism.

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Assay of Progesterone by Intrauterine Application in the Rabbit.

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The crop gland test for the lactogenic hormone as performed by Lyons and Page,¹ the local feather test for estrone by Greenwood and Blyth,² and the intravaginal test for estrogenic substance by Yerby,³ serve as examples of the efficacy of the local application of a hormone for analytical purposes. The application of progesterone to the uterus has been shown by McGinty, Anderson and McCullough⁴ to be a more sensitive test for its presence than introducing the hormone into the blood stream.

Previous biological assay or test procedures for the presence of progesterone have involved the subcutaneous or intramuscular injection of the hormone over a period of 5 days, removal of the uterus on the sixth day and subsequent histological examination of the uterus. The criterion of the activity of the hormone of the corpus luteum was the degree of progesterational proliferation in evidence in

¹⁰ Hartman, C. G., Firor, W. M., and Geiling, E. M. K., *Am. J. Physiol.*, 1930, **95**, 662.

¹¹ Smith, P. E., Dotti, L. B., Tyndale, H. H., and Engle, E. T., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 247.

¹ Lyons, W. R., and Page, E., *Proc. Soc. Exp. Biol. and Med.*, 1935, **32**, 1049.

² Greenwood, A. W., and Blyth, J. S., *Quart. J. Exp. Physiol.*, 1935, **25**, 267.

³ Yerby, D., *Proc. Soc. Exp. Biol. and Med.*, 1937, **36**, 496.

⁴ McGinty, D. A., Anderson, L. P., and McCullough, H. B., *Endocrinol.*, 1939, **24**, 829.