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# Hypoglycemia and Increased Insulin Sensitivity Following Hypothalamic Lesions.*

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An occasional demonstrable fall in the blood sugar level, in the dog, following traumatic transverse lesions in the hypothalamus at the level of the optic chiasm was observed by us[1] (see 1, Fig. 1a). Later profound hypoglycemic crises were encountered, also occasionally, when the ventral third or half of the hypothalamus was severed free by a sweeping semicircular cut made with a small blunt instrument[2] (see 2, Fig. 1a). Subsequently Ingram and Barris described persistent mild hypoglycemia and increased insulin sensitivity following bilateral lesions placed in the region of the paraventricular nuclei in the cat.[3]

The question as to the mechanism involved in the precipitation of hypoglycemia, particularly the crises, has attracted our active attention. Below are interpretations drawn from the results obtained thus far in the investigation. The results pertain to experiments on a large series of dogs.

The possibility of the hypothalamic lesions eliminating a normally tonic descending innervation (brainstem) is ruled out on the basis of the following observations: (1) hypoglycemia was precipitated only occasionally by what appeared to be identical lesions; (2) in no instance was hypoglycemia precipitated by lesions that severed the dorso-caudal hypothalamic connections (see 3, Fig. 1b); and (3) crises occurred characteristically in the presence of bilateral vagotomy as well as bilateral abdominal sympathectomy.

The possibility of a descending (brainstem) innervation being activated, either by release or by irritative effects of the lesions, is tentatively ruled out by the failure of vagotomy or sympathectomy to protect against the crises. However, the crucial experiment in this respect has not been carried out, namely, experiments involving both vagotomy and sympathectomy.

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1 D'Amour, M. C., and Keller, A. D., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 772.

2 Keller, A. D., Noble, W., and Keller, P. D., *Am. J. Physiol.*, 1935, **113**, 79.

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

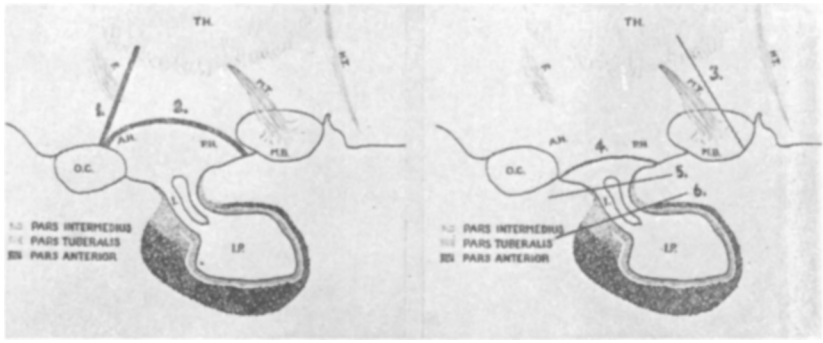


FIG. 1.

Schemata of the hypothalamus and hypophysis of the dog. For explanation of procedures 1 to 6 see text. o.c., optic chiasm; f., fornix; a.h., anterior hypothalamus; p.h., posterior hypothalamus; th., thalamus; m.t., mammillothalamic tract; m.b., mammillary body; h.t., habenular tract; i., infundibulum; and i.p., infundibular progress.

The possibility of the hypothalamic lesions eliminating a normally tonic hypothalamico-hypophysial innervation is ruled out on the basis of the failure of hypoglycemia to follow the separation of hypophysis from the hypothalamus by the following procedures, (1) section of the hypophysial stalk at any level,[4] (see 5 and 6, Fig. 1b), and (2) severing all hypothalamico-hypophysial nerve fibers as they pass through the extreme ventral portion of the hypothalamus, *i. e.*, before their entrance into the infundibulum, (see 4, Fig. 1b). In instances these procedures have been accomplished *with no change in insulin sensitivity,* however, a persistent milk increase (from 2 to 4 times) is exceedingly prone to result.†

Assuming that these experiments were not complicated by as yet unrecognized factors, there remains the possibility that hypoglycemia and increased insulin sensitivity following hypothalamic lesions is precipitated either by the activation of a normally atonic hypothalamico-hypophysial innervation, or by the *derangement of a purely hypophysial mechanism,* induced by immediate neighboring traumatic hypothalamic procedure. The possibility of an endocrine factor common to both the hypophysis and hypothalamus should also be borne in mind.

[4] Keller, A. D., Noble, W., and Hamilton, J. W., *Am. J. Physiol.*, 1936, **117**, 467.

† In the cat increase in insulin sensitivity following procedures 4 and 5 has ranged from 2 to 20 times. Typical marked obesity with no change in insulin sensitivity has been encountered in several instances in the dog following procedure 4.