Neurosecretion Following Hypophysectomy. (18315)

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Elucidation of the various factors controlling the pituitary gland has been a major problem of science for many years. Harris (1) has admirably reviewed the literature concerning the neural control of the hypophysis. His statement, "The pars distalis of the pituitary may in general terms be described as a gland under nervous control but lacking a nerve supply," most aptly phrases one of the oldest problems of neuro-endocrinology, and the same statement may well be extended to parts of the hypothalamico-hypophyseal system other than the pars distalis. However, a careful survey and analysis of the literature reveals that in addition to a direct neural control via nerve fibers at least three additional controlling or influencing mechanisms are known or postulated. They are: (A) a hypothalamico-hypophyseal portal system(2-5); (B) the reciprocal reactions and related functions of parts of the hypophysis to the other endocrine glands (literature too numerous to list); (C) and last, the fact that secretory material elaborated by the hypothalamic neurons may pass to the hypophysis via neurons or by way of the perineuronal spaces(6,7).

Although Scharrer and co-investigators have thoroughly covered the morphological aspects of neurosecretion, extremely little or virtually no experimental observation has been undertaken in the field of neurosecretion. This is especially true in the vertebrates. Speidel(8) conducted some of the earliest experiments on neuro-secretion, using skates as an experimental animal, with negative results. The only positive evidence so far published regarding the relationship of neurosecretion to any other physiological processes of the vertebrate has been offered by Drager (9). A full report of this work with additional experimental evidence is in preparation.

In certain neuro-endocrine studies of the tropical indigo snake, *Spilotes corais*, the animals were hypophysectomized according to a method described previously(10), and following hypophysectomy the empty sella turcica was packed with fibrin foam. Animals so treated were sacrificed at 2, 3 and 4 weeks postoperatively. The fibrin foam and brain were removed, fixed, sectioned serially and stained by Foot's modification of the Masson method. In species of this animal sacrificed 3 weeks after hypophysectomy the supra-optic nucleus is not completely degenerated and contains a small amount of neuro-secretory material. Furthermore, in animals sacrificed at 2 and 3 weeks postoperatively, the fibrin foam within the empty sella contains an appreciable number of spherical granules. The staining characteristics of these granules are identical to the secretory granules within the nerve cells of the hypothalamus. On the basis of staining characteristics and following the comparison of these granules with the secretion from and within the nerve cells of the supra-optic nucleus, there can be little doubt that such granules come from the hypothalamic neurons and pass along the hypothalamico-hypophyseal nerve tract to be lodged in the fibrin foam within the sella (Fig. 1, 2, and 3).

As the granules pass toward the pituitary they maintain close relationship to the nerve

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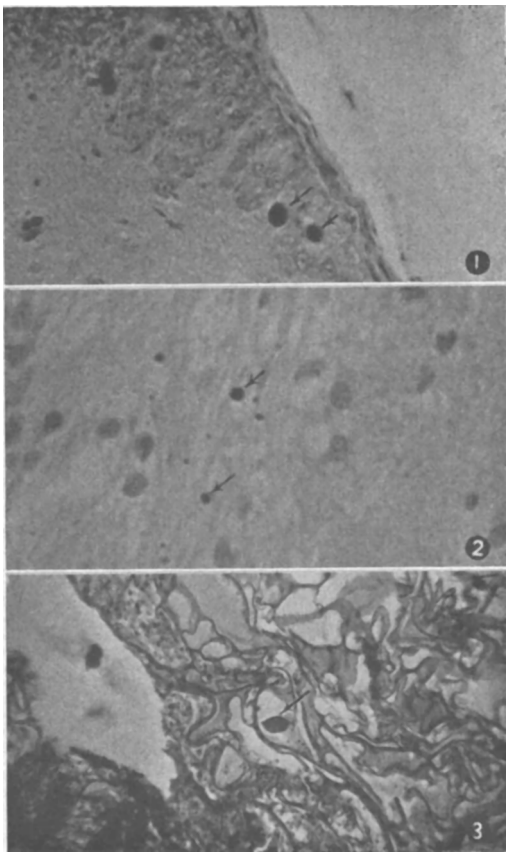

FIG. 1. Secretory material, indicated by arrows, within the supra-optic nucleus of the intact animal.

FIG. 2. Arrows indicate several secretory granules dispersed along the hypothalamico-hypophyseal nerve tract of the intact animal.

FIG. 3. Secretory granule lodged in the fibrin-foam.

fiber tract and apparently follow the perineural spaces to the hypophysis.*

It has been questioned whether the so-called "granules of Scharrer" were not merely artifacts of colloid which had migrated "up stream" along the hypothalamico-hypophyseal nerve tract.† This experiment strongly indicates that the "granules of Scharrer" from the magnocellular portion of the hypothalamus reach the hypophyseal region in the absence of the pituitary gland. Under conditions described it seems impossible that these granules can be upward migratory products from the hypophysis and therefore such secretions can hardly be the products of degeneration as once postulated. The foregoing statement is substantiated by Drager (9) when it was found that extirpation of all the endocrine glands had little or no effect on the hypothalamic neurons, yet hepatectomy invariably produced a marked decrease in the secretory granules and a vacuolation of the cells in the magnocellular portions of the hypothalamus.

Although the fact exists that secretory products from the hypothalamus traverse the hypothalamico-hypophyseal tract, few investigators of the hypophysis recognize this as a possible controlling mechanism of the pituitary gland. However, considerable evidence now points in this direction.

* In the average (normal) animal the granules may be observed in the large cells of the hypothalamus, along the hypothalamico-hypophyseal nerve tract and in the posterior lobe of the pituitary. In the toad such granules are often present in the intermediate lobe of the hypophysis.

† Bargman and Held, investigating dogs and cats, have traced the secretion products of the supra-optic and para-ventricular nuclei to the pars nervosa. These investigators interpret the bodies of Herring as hypothalamic secretory condensations in the posterior pituitary. No experimental evidence is offered for their conclusions. *Acta. Anat.*, 1949, v7, 264.

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