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Venous Outflow of the Hormones Secreted by the Rat Pituitary Autotransplanted Beneath the Kidney Capsule[1] (39452)

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The rat hypophysis, when transplanted beneath the kidney capsule, will secrete elevated amounts of prolactin for an extended period (1-3). A low level of luteinizing hormone (LH) and follicle stimulating hormone (FSH) release, which can be enhanced by chronic treatment with LH-releasing hormone, appears to persist for at least 16 days following renal transplantation (4). The vascular connections of the transplant with the general circulation have not been adequately defined, although the renal artery has been implicated as the efferent vessel (5). The prospect of using this ectopic pituitary preparation as a model to investigate the release of LH and prolactin in response to various stimuli led us to determine whether its hormones were secreted into the renal vein. In these studies, jugular venous levels of the hormones were taken to represent their concentration in the peripheral circulation.

Materials and methods. Adult Holtzman (Sprague-Dawley) male or female rats were hypophysectomized under ether anesthesia by the parapharyngeal approach and studied either as such or after pituitary autotransplantation. In the latter case, the whole pituitary, recovered from a trap bottle in the suction line, was placed under the left kidney capsule immediately after hypophysectomy. A small number of intact regularly cyclic female rats in diestrus was also studied. The rats were kept under controlled light (14-10 hr light:dark) and temperature (76°F) conditions, with free access to Purina laboratory chow and tap water. At various intervals after the operation the rats were lightly anesthetized with ether, and 1 ml or less of blood was removed by jugular venipuncture. In addition, one group of pituitary autotransplanted rats was killed 8 days after operation, just after sampling the jugular vein, by exsanguination through the left renal vein. The remaining autotransplanted rats were killed 4 weeks after operation, when blood samples were taken simultaneously from the jugular, right, and left renal veins.

Completeness of hypophysectomy was ascertained by macroscopic examination of the pituitary fossa and atrophy of the adrenal glands and gonads. The blood samples were permitted to clot at room temperature, then centrifuged at 4°, and the serum was stored at −20° until assayed. The serum from each sample was assayed in duplicate for prolactin and LH by specific radioimmunoassays (6, 7). The LH values were expressed in terms of rat LH standard LER-1240-2 (0.6 × NIH-LH-S1); prolactin values were expressed in terms of rat prolactin standard LER-1382-82 (45.7 IU/mg).

Results. The results are summarized in Table I. The LH levels in the jugular vein serum of the hypophysectomized-pituitary autotransplanted rats were not significantly different from those found in the renal vein serum and did not seem to be affected by the sex of the host or by the interval after operation. Although the values were about half of those found in the intact diestrous females, none of them fell below the minimal detectable level of the assay (0.15 ng/ml). In the hypophysectomized rats, however, all the values were found to be below the minimal detectable level by the third week after operation, although a mean value of 0.22 ng/ml was found 1 week after operation.

The prolactin levels in the jugular vein serum of the hypophysectomized-pituitary autotransplanted rats were also indistin-

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TABLE I. LEVELS OF PROLACTIN AND LH IN THE JUGULAR AND RENAL VEIN SERUM OF RATS AFTER HYPOPHYSECTOMY OR HYPOPHYSECTOMY PLUS PITUITARY AUTOTRANSPLANTATION.[a]

Experimental condition	Number of rats[b]	Interval after operation (days)	Serum LH levels (ng/ml)		Serum prolactin levels (ng/ml)	
			Jugular	Renal[c]	Jugular	Renal[c]
Intact, diestrus	4 (F)	–	0.61 ± 0.11	–	7.0 ± 2.0	–
Hypophysectomy	4 (F)	7	0.22 ± 0.01	–	–	–
		21	<0.15[d]	–	–	–
	5 (F)	7	–	–	1.51 ± 0.13	–
		14	–	–	1.55 ± 0.05	–
		21	–	–	1.49 ± 0.03	–
		28	–	–	1.52 ± 0.05	–
Hypophysectomy-pituitary autotransplantation	5 (M)	8	0.30 ± 0.3	0.29 ± 0.03	76.1 ± 29.6	30.2 ± 6.2
	5 (F)	8	0.32 ± 0.04	0.29 ± 0.04	51.5 ± 11.0	48.9 ± 6.6
	10 (F)	0[e]	2.85 ± 0.25	–	53.0 ± 8.7	–
		7	0.32 ± 0.03	–	73.3 ± 5.1	–
		14	0.38 ± 0.04	–	45.4 ± 3.4	–
		21	0.36 ± 0.04	–	44.1 ± 2.4	–
		28	0.36 ± 0.03	0.39 ± 0.05[f]	41.7 ± 3.8	48.3 ± 5.5[g]

[a] Values for prolactin and LH are in all cases means and SEM.

[b] Sex of the subjects indicated in parentheses.

[c] The vein draining the pituitary transplant-bearing kidney; in all cases this was the left one. The *LH standard* was LER-1240-2 (0.6 × NIH-LH-S1); the *prolactin* standard was LER-1382-82 (45.7 IU/mg).

[d] The minimal detectable level was 0.15 ng/ml; in all cases the level was below this minimum.

[e] Sampled immediately before operation.

[f] The LH level in the right renal vein was 0.4 ± 0.04.

[g] The prolactin level in the right renal vein was 42.7 ± 3.7.

guishable from those found in the renal veins of either kidney and were also unaffected by the sex of the donor or the interval after operation. They were many-fold higher than the values found in either the intact diestrous rats or those subjected only to hypophysectomy.

Discussion. The hormones secreted by the transplanted pituitary, thus, do not appear to be secreted into the renal vein. The transplant is apparently vascularized by the blood vessels of the capsule, to which it forms a firm attachment. The blood supply of the renal capsule has not been exactly identified in the rat, but it is probable that the major venous drainage is the same as that of the parietal peritoneum, i.e., the phrenico-abdominal and cranial abdominal veins on the right and left sides, respectively. These empty into the inferior vena cava just cranial to the renal veins (8).

The finding of high serum prolactin levels in hypophysectomized-pituitary autotransplanted rats in neither surprising nor new. The fact that the LH levels were slightly but significantly higher than after simple hypophysectomy, up to at least 4 weeks after operation, however, suggests that LH secretion is not completely prevented by separation of the pituitary from its normal connections to the hypothalamus. This conclusion is also supported by the recent finding of low basal levels of LH in the hypophysectomized rat bearing a homotransplanted pituitary from a long-term ovariectomized donor (9); these levels, however, were not compared with those of rats subjected to hypophysectomy alone. The most immediate importance of the finding that LH can be secreted in small amounts by the transplanted pituitary is the reservation which this imposes on the experimental use of the transplanted pituitary to study the effects of prolactin separate from any possible effect of LH.

Summary. In adult female or male rats subjected to hypophysectomy and autotransplantation of the pituitary beneath the renal capsule, the levels of prolactin in the renal vein of the pituitary-bearing kidney were not significantly different from those found either in the renal vein of the contralateral kidney or in the jugular vein. LH levels were slightly but highly significantly higher than those found in hypophysectomized rats; the levels found in the two renal veins and the jugular vein were also not significantly different from one another.

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