Blood flow and autoregulation in rat pituitary gland

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The authors describe an experimental model that allows dynamic studies of blood flow in the pituitary gland. Twenty-eight male Wistar rats were anesthetized and the pituitary gland was exposed using a parapharyngeal approach. Teflon-coated platinum wire electrodes were placed in the adenohypophysis near the midline and laterally as well as in the parietal cortex and the white matter. Blood flows were measured by the hydrogen clearance method. Baseline values were as follows: 89.9 ± 22 ml/100 gm/min in the medial adenohypophysis, 55.9 ± 8 ml/100 gm/min in the lateral adenohypophysis, 59.2 ± 14 ml/100 gm/min in the parietal cortex, and 28.1 ± 8.9 ml/100 gm/min in the white matter. Effective autoregulation was demonstrated by altering the blood pressure with metaraminol infusion or blood withdrawal. The range of autoregulation was wider in the adenohypophysis than in the cerebral cortex.

KEY WORDS - pituitary gland • rat • autoregulation • blood flow

Since early investigations on pituitary anatomy first revealed the portal system, research on pituitary blood flow has been almost entirely concerned with its direction, while quantitative aspects of perfusion have been largely ignored. In 1961, Goldman suggested that “The regulation of at least some endocrine activity of this gland may be inversely related to the vasomotor modulation of its perfusion.” However, it was only the concept of neurosecretion that drew attention to quantitation of pituitary blood flow, since the amount of a neurosecretory product reaching its destination is proportional not only to secretion but also to local blood flow. Measurement of pituitary blood flow by the commonly used diffusible indicator, rubidium-86, or radiolabeled microsphere technique is unreliable because of the special angiostructure in this gland, and does not allow for dynamic studies.

In our present study, the hydrogen clearance method was used, with a direct approach to the pituitary gland, to establish the limits of autoregulation in the adenohypophysis of rats.

Materials and Methods

Twenty-eight male Wistar rats, weighing 270 to 300 gm each, were used in this investigation. Food and water were given freely until the beginning of the experiment. Anesthesia was induced by a short period of ether inhalation and was maintained with intraperito-
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Fig. 1. Diagram of the experimental model. mPBF = blood flow in the medial part of the adenohypophysis; lPBF = blood flow in the lateral part of the adenohypophysis.

of the bone and the dura were removed with fine watchmaker’s forceps. The ventral surface of the anterior pituitary gland was exposed in the same manner, and two platinum electrodes similar to those placed in the cortex and white matter were inserted into the adenohypophysis, one in the midline and one laterally. It was necessary to cut the tip of the electrodes obliquely to facilitate penetration of the tissue. The depth of penetration was easily controlled under direct vision. The tip of the electrode and 0.1 mm of its insulated length were introduced into the tissue. A reference electrode (sintered silver/silver chloride) was placed subcutaneously (Fig. 1). All manipulations were performed with the aid of an operating microscope.†

Blood flow was measured using the hydrogen clearance method. Polarizing voltage was applied and the system was allowed to stabilize. Hydrogen gas was mixed with the inspired air via the endotracheal tube to reach a concentration of about 5% to 7%. The clearance curves were recorded in parallel on four channels. The curves were replotted on semilogarithmic sheets and the flow was calculated using the “initial slope” graphic method.†† Twenty-two rats were used to establish the limits of autoregulation in the adenohypophysis. In these animals, blood pressure was raised by infusion of metaraminol (1 to 8 mg/hr) and lowered by graded blood withdrawal. The arterial blood samples were retained for blood gas analysis. Blood flow was measured at every pressure increase or decrease.

The remaining six rats were used as a control group. The same surgical procedure was carried out, but the blood pressure was kept stable over a period of 2 to 3 hours to detect possible spontaneous changes in blood flow.

To facilitate histological confirmation of the localization of the electrodes, small coagulation lesions were made by applying 9 V direct current potential between the reference electrode and each active electrode before removal. The animals were then decapitated, and the brain and the pituitary gland were removed and stored in 10% buffered formalin.

Results

Control Animals

Baseline values were established using the six control animals. Average mean arterial blood pressure at the beginning of recording was 95 ± 6 mm Hg. Blood flow measured by the “cortical” electrode was, of course, a mixed cortical-white matter flow and was in the range of 59.2 ± 14 ml/100 gm/min. White matter flow was 28.1 ± 8.9 ml/100 gm/min. Blood flow in the adeno-

† OPMI 6H-SF operating microscope manufactured by Carl Zeiss, Inc., 44 Fifth Avenue, New York, New York.
TABLE 1
Summary of blood flow findings in 22 animals at various blood pressure levels*

<table>
<thead>
<tr>
<th>Blood Flow (ml/100 gm/min)</th>
<th>Blood Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
</tr>
<tr>
<td>medial adenohypophysis</td>
<td>34†</td>
</tr>
<tr>
<td>lateral adenohypophysis</td>
<td>21†</td>
</tr>
<tr>
<td>cortex</td>
<td></td>
</tr>
<tr>
<td>white matter</td>
<td>15†</td>
</tr>
</tbody>
</table>

* Values are means ± standard deviations. Blood gases were continuously monitored and were within the following ranges at each blood pressure level: pCO2, 4.3 to 5.4 kPa; pO2, 11.9 to 12.5 kPa.
† Values were obtained from one animal only.

hypophysis depended on the position of the electrode: in the midline it was 89.9 ± 22 ml/100 gm/min, and in the lateral part it was 55.9 ± 8 ml/100 gm/min. These values were remarkably stable over the recording period of 2 to 3 hours. In a few early experiments very high flow values (greater than 200 to 400 ml/100 gm/min) were recorded in the midline. It was confirmed later that the electrodes were placed too deeply and were chiefly recording the neurohypophyseal flow. These experiments were excluded from the study.

Experimental Animals

In testing the upper limits of autoregulation, it was very difficult to raise the mean arterial blood pressure above 170 mm Hg because the animals developed cardiac arrhythmias and only a few recordings were obtained. The results are summarized in Table 1 and Fig. 2 left. In the medial adenohypophysis, blood flow measurements showed a good autoregulatory plateau in the mean arterial blood pressure range of 40 to 140 mm Hg (slope $A_1 = 0.195$ ml/100 gm/min/torr). Above and below this range the blood flow was progressively more pressure-dependent. In the lateral adenohypophysis, good autoregulation was noted within the mean arterial blood pressure range of 40 to 170 mm Hg (slope $a_1 = 0.065$ ml/100 gm/min/torr). Blood flows measured at the extremes of the autoregulatory plateaus (40 to 140 mm Hg and 40 to 170 mm Hg, respectively) were not significantly different ($p > 0.1$, Student t-test).

Blood flows in the cortex (Fig. 2 right) remained fairly stable at mean arterial blood pressures between 60 and 130 mm Hg (slope value $A_2 = 0.183$ ml/100 gm/min/torr), and any differences between cortical blood flow recordings were not statistically significant. Below 60 mm Hg and above 130 mm Hg failure of autoregulation was observed. The limits of autoregul-

![Fig. 2. Mean autoregulation curves in 22 rats based on the rise and fall in mean arterial blood pressure (MABP) and blood flow in the medial (mPBF) and lateral (lPBF) parts of the adenohypophysis (left) and in the cortex (CBF) and white matter (WBF) (right). $A_1$ and $a_1$ represent the slopes of the autoregulatory plateaus. Vertical lines indicate standard deviation (SD).](image-url)
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Discussion

Pituitary blood flow and its control are important factors in neural control of anterior pituitary function. It has been shown in earlier studies that variations in perfusion influence the function of some endocrine glands and a similar effect was suspected in the pituitary gland. As new anatomical techniques led to a fuller understanding of the pituitary angiography. and as new physiological methods yielded new concepts of directional pituitary blood flow, it became apparent that adenohypophyseal blood flow could not be studied with the widely used diffusable indicator method or the radio-isotope labeled microsphere technique. It is an accepted view that blood entering the adenohypophysis has to pass first through the neurohypophysis. When using the diffusable indicator method, some indicator will be extracted from the blood in the neurohypophysis before entering the anterior lobe. The same principle applies to the labeled microsphere technique so that some of the microspheres will be filtered out. These methods also have the disadvantage of allowing only one measurement per animal.

Both the hydrogen clearance method, which was used by Porter et al., in a stereotaxic approach to the pituitary gland, and the thermoelectric technique, which Kopaniky and Gann applied in the dog, allow for dynamic testing. The direct approach to the adenohypophysis, which was employed in this study, enables electrode placement to be controlled under direct vision. Blood flow measurements proved to be stable if the animal was left undisturbed, and the values recorded were consistent with those reported by earlier investigators.

Blood flow in the adenohypophysis was found to be higher in the midline than in the lateral lobe. In a few animals the logarithmic transformation of the desaturation curve obtained from the midline had two different components. The first yielded a calculated blood flow greater than 300 ml/100 gm/min, whereas the second was within the usual range of blood flow measured in the adenohypophysis. These results suggested that the electrodes had been placed too deeply, so that they were registering the sum of blood flows in two different compartments, with the slower flow being in the adenohypophysis and the faster in the neurohypophysis (neurohypophyseal blood flow has been measured at values ranging from approximately 220 to 400 ml/100 gm/min). This study provides evidence of effective autoregulation in the adenohypophysis, although the increase in adenohypophyseal perfusion after blood withdrawal seen by Kopaniky and Gann in dogs was not confirmed. Adequate perfusion is maintained at a mean arterial blood pressure as low as 40 mm Hg. The flow is more stable against fluctuating blood pressure in the lateral than in the median portion. We submit that the results described in this paper establish the limits of autoregulation in the adenohypophysis of the rat, and show the limited effect of alterations of arterial blood pressure on blood flow in the pituitary gland.

References


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