THE HYPOTHALAMIC FACTOR INFLUENCING SECRETION OF THE LUTEINIZING HORMONE OF THE ANTERIOR HYPOPHYSEAL LOBE

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There is a widely held view that nervous regulation of the hypophysis is mediated by substances contained in the hypothalamic neurosecretion. However, more or less convincing physiological evidence of the relationship between the anterior lobe secretory activity and the substances elaborated within the hypothalmus is available only in so far as influences on the adrenocorticotropic function are concerned [1, 2].

In our laboratory a systematic study is being made of regulation by the hypothalamus of anterior hypophyseal lobe gonadotropic function, particularly in connection with secretion of the luteinizing hormone (LH). It has been shown that electrical destruction of certain regions of the hypothalamus does not impair the production of LH but does interfere with secretion from the hypophysis [3]. It has also been shown that an extract of hypothalamus or a suspension of posterior hypophyseal lobe induces ovulation in adult females, disturbance of the sexual cycle, and prolonged menses during which time no ovulation occurs; it also causes ovulation in sexually immature females which had previously received an injection of follicle-stimulating hormones to cause pre-ovulatory development of follicles [4]. From these results we may conclude that in the hypothalamus and in the posterior hypophyseal lobe there is a factor which either itself elicits ovulation, or else makes possible the liberation of LH from the hypophysis. McCann and Taleisnik [6, 7, 8] made a series of studies whose results in their opinion indicate the presence of a hypothalamic factor influencing the secretion of LH.

However, from the results obtained by these same authors [7], the reaction of reducing the ascorbic acid in the ovaries, which they used as an index of the secretion of LH, and which they took as specific, is also observed in hypophysectomized animals after an injection into them of hypothalamus or of vasopressin. The reaction must, therefore, be nonspecific and the value of results gained by it must be thrown in doubt.

Some confusion has also been caused over the question of the existence of a hypothalamic factor influencing LH secretion by the experiments of Courrier et al., [5] who also estimated the influence of hypothalamic extracts in terms of the reduction of ascorbic acid in the ovaries.

Therefore, to settle the problem of the existence in the hypothalamus of a substance or substances influencing the luteinizing function of the hypophysis additional experiments are required in which hypothalamic preparations are tested not only under conditions when the secretion of endogenous reaction is completely excluded, but when the influence of this hormone could be inferred from reactions specific to it.

In the present communication we report the results of the test of preparations of hypothalamus and posterior hypophyseal lobe on hypophysectomized animals; in this work we have used the occurence of ovulation as a more specific indication of the action of the luteinizing hormone.

METHOD

The experiments were carried out on young female hypophysectomized rats weighing 35-40 g.

The test preparations – an extract of hypothalamus or a suspension of posterior hypophyseal lobe – were in some experiments injected immediately after extirpation of the hypophysis and in others one or two days after this operation.

Results of a Test of an Extract of Hypothalamus or Posterior Hypophyseal Lobe on the Ovulation Reaction in Hypophysectomized Infant Female Rats Injected with Pregnant Mare Serum

Preparation	Sex of donor	Dose	Number of recipients		Number of ova in both oviducts
			Total	Responded by ovulation	
Hypophysectomized recipients					
Extract of hypothalamus	♂♂	2.0*	3	0	–
Ditto	♀♀	2.5*	8	0	–
Suspension of posterior hypophyseal lobe	♀♀	2.0*	8	0	–
Suspension of anterior hypophyseal lobe	♀♀	2.0*	4	4	35, 13, 23, 18
Chorionic gonadotropin	–	20-40	4	3	18, 42, 37
Recipients with subtotal hypophysectomy					
Extract of hypothalamus	♀♀	2.0*	3	2	8, 5
Suspension of posterior hypophyseal lobe	♀♀	2.0*	1	1	7
Recipients with mock hypophysectomy					
Extract of hypothalamus	♂♂	2.0*	1	1	4
Ditto	♀♀	2.0*	5	3	22, 17, 4
Suspension of posterior hypophyseal lobe	♀♀	1.0*	7	6	14, 19, 8, 1, 17, 4

*Equivalent number of rat hypothalami or hypopheses per recipient.

The first of these preparations was injected into the jugular vein and the second intraperitoneally (preliminary experiments on animals with an intact hypophysis [14] showed that these methods of injection were effective).

To stimulate three ovulatory ovarian follicular growth, 56 hours before the injection of one or the other of these preparations (i.e., 8-56 hours before hypophysectomy), subcutaneous injections of pregnant mare serum were given. This preparation by itself, even in large doses does not cause ovulation under these conditions [10]. The post mortem examination was made 18-24 hours after the injection of hypothalamic or of hypophyseal preparations, in order to determine the reaction. To test whether the ovaries had not lost the power of ovulation during the short interval after hypophysectomy the hypophysectomized animals of the two control groups which had also received pregnant mare serum were also injected with preparations containing LH (either chorionic gonadotropin or a suspension of anterior hypophyseal lobe). Another group of control animals were subjected to a control operation in which the hypophysis was left intact. One more control group consisted of a few individuals from whom the hypophysis had been incompletely removed.

The hypothalamus and posterior hypophyseal lobe were taken from adult animals (females in the period of diestrus, or males).

The extract was made by triturating several hypothalami with quartz sand in 0.1 N HCl followed by centrifugation; the volume was made up with same HCl solution to 0.5 ml per recipient. Aqueous suspensions of the posterior or anterior hypophyseal lobe were prepared.

In a positive reaction, at the ovarian end of the oviduct, examination under the binocular microscope revealed a transparent segment containing an accumulation of ova. The ova were removed from the oviduct by a method described previously [3], and the number counted.

EXPERIMENTAL RESULT

Previously [4] it has been shown that in a normal infant female rat, in which an injection of pregnant mare serum had already induced the development of follicles, injection of hypothalamic or posterior hypophyseal lobe preparation (under the same conditions and at the same times as in the present work) induced ovulation in a considerable number of the individuals.

The results of the experiments shown in the table, with a mock hypophysectomy of such females indicates that the surgical trauma related to the operation does not by itself disturb the links in the chain of processes leading to ovulation.

In the control groups, in the completely hypophysectomized animals which had received either chorionic gonadotropin or anterior lobe extract, in most cases there was a strong ovulatory reaction with the liberation of a large number of ova. This indicates that at least in the first three days after hypophysectomy the ovaries were still able to respond to LH by ovulation. At the same time the hypothalamic and posterior lobe extracts caused no ovulation in any of the hypophysectomized females. A positive response was found only in those which were substotally hypophysectomized.

It has been known that the injection of a hypothalamic extract or suspension of posterior hypophyseal lobe into infant females in which follicular development had previously been induced is a sufficient stimulus to evoke ovulation [4].

It may be supposed that these preparations either act directly on the ovary, i.e., contain a sufficient amount of luteinizing hormone to induce ovulation, or else that they stimulate the secretion of this hormone from the hypophysis.

The results of our experiments eliminate the possibility that under these conditions ovulation results from the direct action of the preparation on the ovaries. Indeed in the absence of a hypophysis neither a hypothalamic extract nor a suspension of posterior hypophyseal lobe caused ovulation. Control experiments with the injection into the hypophysectomized animals of a preparation known to contain a luteinizing hormone (ethorionic gonadotropin or a suspension of anterior hypophyseal lobe) afford convincing proof that in the short time of the hypophysectomy the follicles which had previously developed in the ovary do not lose a sensitivity to the LH and are able to react to it by ovulation.

We may, therefore, take it as established that a factor is contained in the hypothalamus and posterior hypophyseal lobe which can induce the secretion of the luteinizing hormone from the anterior lobe.

Nikitovitch-Winer [9] came to the same conclusion; in her experiments the rats in which spontaneous ovulation had been blocked by pentobarbital were also caused to ovulate by the injection of a hypothalamic extract directly into the hypophysis.

SUMMARY

As demonstrated by the previous communication, administration of acid aqueous extract from hypothalamus or suspension of the posterior hypophyseal lobe to female rats whose ovaries had mature follicles, resulted in ovulation (Kabak and Sokolova, 1962). The paper presents the results of further investigations in which the same preparations of the posterior hypophyseal lobe or hypothalamus were administered during the first two days after hypophysectomy. Experiments were staged on infantile female rats which received gonadotropin from the pregnant mare serum to stimulate the preovulation growth of the follicles. In contrast with the females with intact hypophysis no ovulation was caused in hypophysectomized female rats either by hypothalamic extract, or by a posterior hypophysis lobe suspension. These data demonstrate that the hypothalamus and the posterior hypophysis lobe contain one or several substances stimulating the luteinizing hormone secretion by the anterior hypophysis lobe.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
