DEVELOPMENT OF INTRALIENAL TRANSPLANTS OF OVARY UNDER CONDITIONS OF MECHANICAL STIMULATION OF THE HYPOTHALAMUS

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As we know, intralienal transplants of ovary serve as a source of an experimental model of ovarian tumors [1, 3, 6]. In a previous work, it was shown that vegetotropic substances exert a substantial influence on the growth and development of intralienal transplants [1]. The role of the vegetative centers of the hypothalamus was investigated in experiments with electrical and mechanical stimulation of the hypothalamus [5].

In this work, we present data on the development of intralienal transplants of the ovary during mechanical stimulation of the hypothalamus.

EXPERIMENTAL METHOD

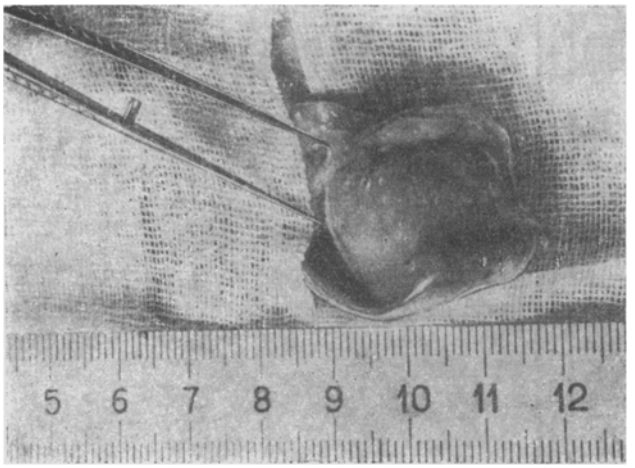
The experiments were set up on 42 non-pedigreed white, female rats. After castration, an autoplastic transplantation was performed, placing a fragment of ovary (6 mm^2 in size) under the capsule of the spleen. Bilateral mechanical stimulation of the hypothalamus was performed by the insertion of glass pellets, 1-1.5 mm in diameter. In the first series of experiments (28 animals), the pellets were inserted either simultaneously with transplanting or 2 days after it. In the second series of experiments (14 animals), the ovarian transplantation was performed first, then, after 2 or 6 months, the growth of the transplants was checked by exploratory laparotomies, and after this the glass pellets were inserted into the hypothalamus of the animals. In the control animals (17 rats), only transplantation of the ovary into the spleen was performed. During the course of the experiment the sizes of the transplants in the experimental and control animals were compared according to area.

In one of 2 special series of experiments we studied the gonadotropic reaction, and in the other – the concentration of gonadotropic hormones in the tissue of the rat adenohypophysis with insertion of pellets in the hypothalamus. The hypophyses were tested in infantile rats, according to the widely accepted method [2]. In this series of experiments we used 20 animals with equal development intervals of the transplants (analogous to the intervals of the first series), and 20 animals with longer intervals (greater than 3 months). Pellets were inserted into the hypothalamus in half the animals of this series, and the remaining animals served as the control. In addition, in this series we studied the concentration of gonadotropic hormones in the hypophysis of 10 intact rats and 10 other rats, also without transplants but with pellets inserted in their hypothalamuses. In evaluating the results, we calculated the ratio of the weight of the ovaries to the weight of the body of the infantile rats in which we tested the hypophyses of the experimental and control animals. The numerical data was analyzed statistically.

The gonadotropic reaction was studied in 20 infantile rats, of which pellets were inserted in the hypothalamus of 14 and 6 served as controls. The experimental and control animals received equal quantities of S.A.F. In evaluating the results, we compared the weight of the sexual apparatus in the experimental and control animals.

EXPERIMENTAL RESULTS

The experiments of the first series showed that mechanical stimulation of the hypothalamus, performed 2 days after the operation, leads to a sharp inhibition of growth, down to complete resorption of the transplant. Thus, on exploratory laparotomy, performed 2 months after transplantation, it was observed that 10 of the 18 ovarian transplants were completely resorbed, and the remaining 8 showed no growth: in three animals the size of the transplant was



External appearance of the tumor in the spleen of a rat.

equal to its measurements at the time of transplantation, and in 5 it had decreased.

Six months after the operation the animals were sacrificed. In 21 of the 28 rats, the transplant in the spleen was not found; transplants were seen in only 7 rats, and only in one did it attain a size of 24 mm^2.

Investigating the location of the glass pellets (in sections impregnated with silver according to Campos) showed that in the majority of animals they were placed in the bounds of the hypothalamic region – in the mammillary, ventromedial, conjunctive, and tuberal nuclei. In addition, in a portion of the animals the pellets were situated in areas adjacent to the hypothalamus (ventral and lateral nucleus, hypocampus). In determining the neural structures in which the glass pellets were situated, we used Krieg's atlas of the rat's brain [8] and also the atlas of Fifková and Marsala [7].

In the control animals the transplants enlarged progressively, and by the sixth month their mean size had reached 13 mm^2 (with $P < 0.001$).

In the second series of experiments, only in 2 of the 14 animals did we find remnants of a degenerating yellow body at the site of the transplant, with infiltrating, segmentonuclear leukocytes and surrounding hyalinized connective tissue. In 3 rats the transplants had not grown in size. In the remaining 9 rats, following insertion of pellets in the hypothalamic region, we noted appreciable activation of the transplant growth. Thus in one of them, prior to the operation in which the pellets were inserted, the size of the transplant was equal to 156 mm^2, and after 3 months the transplant had doubled in size. One of the pellets was found in the mammillary nucleus, the other in front of the ventromedial nucleus. Histolo ical investi ation showed that the base area of the transplant consisted of a thecoma; a small nodule of ovarian tissue with corpora lutea of normal structure was found in its surface (see figure).

In another animal of this group the size of the transplant before the pellet implantation operation was 15 mm^2, while after $3\frac{1}{2}$ months the transplant attained a size of 240 mm^2, and on histological investigation was seen to be a luteoma. Both pellets were found in the region of the mammillary bodies. On histological investigation, the remaining transplants were shown to be three luteomas with growth of the follicular epithelium; out of these, one of the rats had a mixed tumor – luteoma plus folliculoma. The remaining 4 transplants were essentially lutein tissue; in one case we noted infiltration of the transplant tissue with segmentonuclear leukocytes.

The results of the special series of experiments showed that the presence of pellets in the hypothalamus of rats with 2-wk old ovarian transplants leads to a statistically significant elevation in the concentration of gonadotropic hormones in the hypophysis (the weight of the ovaries in the infantile rats, in which the hypophyseal tissue was tested, was equal to 34 mg, as compared to 13.7 mg in the animals that only had the ovarian transplant, with $P < 0.01$). In the animals that had the ovarian transplantation 3 months before implantation of the pellets the latter did not exert a stimulatory action on the concentration of gonadotropins in the hypophysis.

It is interesting to note that the insertion of pellets into the hypothalamus of rats that did not have ovarian transplants led, on the other hand, to a significant lowering of the concentration of gonadotropic hormones in the hypophysis, as compared with the intact rats.

The gonadotropic reaction in the animals with pellets inserted in the hypothalamus was seen to be inhibitory. Thus, in the intact infantile rats that received S.A.F. the weight of the sexual apparatus ranged from 79 to 85 mg, while in the experimental group – from 38 to 60 mg.

Thus, mechanical stimulation of the hypothalamus led to a sharp inhibition of the transplant's initial growth, despite the increase in the concentration of gonadotropins within the hypophysis, while at late stages in the development of the transplant it caused stimulation of the growth (although the concentration of gonadotropins in the hypophysis did not change).

It could be postulated that, under the conditions of our experiment, there occurred a retention of the gonadotropic hormones in the hypophysis and,therefore, they did not gain access to the blood stream. However, in the special series of experiments on infantile rats, in which pellets were inserted in the hypothalamus, it was shown that the sensitivity of the ovarian tissue to gonadotropin under these conditions is lowered. If you add to this the fact that denervation of the ovary also lowers its sensitivity to gonadotropin [1], and that, as a result of this, the intralienal transplant reacts weakly to gonadotropins [4], then the data of the first series of experiments may be treated as the result of a sharp drop in the sensitivity to gonadotropins of the ovarian tissue transplanted to the spleen. Apparently, under the conditions of our experiments, the hypothalamic effects are realized primarily by a change in the sensitivity to the gonadotropic hormones, and not by a change in the quantity of these hormones.

Taking into consideration the change in the functional state of the hypothalamus of rats at the late stages of development of the ovarian transplant [5], as well as the data on the regeneration of nerve connections with the central nervous system along with growth of the transplant [1], it might be expected that the effect of the hypothalamus at these intervals would be different. However, the mechanism of the activating influence, observed in the second series of experiments, needs further experimental analysis.

SUMMARY

Experiments were conducted on castrated albino rats with ovarian transplant in the spleen. Bilateral mechanical irritation of the hypothalamus by implantation therein of glass balls causes resolution of ovarian grafts transplanted simultaneously with implantation of the balls. If, however, the latter procedure was done 6 months after the transplantation it augmented the growth of the transplants. Determination of gonadotropic hormones in the hypophysis of experimental animals showed that the occurring changes could not be attributed to alterations of gonadotropin production.

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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.
