EFFECT OF PROGESTERONE, FOLLICULIN AND CASTRATION ON THE ELECTROENCEPHALOGRAM OF FEMALE RABBITS

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A large amount of experimental and clinical material has been published in recent years on alterations in the state of the nervous system of women during the menstrual cycle and at the menopause, i.e., at times when the amount and the relative proportions of the ovarian hormones undergo change. Thus L. I. Shvang and I. Ya. Romm (2) have reported alterations in the electroencephalogram of healthy women occurring a few days before, and during the first days of menstration.

It is now possible to examine separately the effect on the central nervous system of estrogenic hormones and of the luteal hormone, and such an examination is of importance for obtaining more precise indications for hormone therapy in gynecology.

The object of our research was to study the electrical activity of the cerebral cortex of female rabbits after administration of various doses of folliculin and progesterone, as well as after castration.

EXPERIMENTAL METHODS

Electroencephalograms were recorded from 7 female rabbits, under conditions of series experimentation. Indwelling electrodes were previously implanted into all the animals.

The electrodes, which had been provided with a screw-thread, were screwed through the cranium in the frontal and parietal regions, so that they were in contact with the meninges.

The potentials were recorded using an oscillographic equipment, with a symmetrical amplifier and with electronic registration. The records were taken on moving cinematographic film. The electroencephalograms (EEG) were evaluated visually, by comparing one with another (constant time of the amplifier T = 1.15 seconds).

We usually began the recordings on the 3rd to 4th day after implanting the electrodes, and the recordings were taken twice daily for one animal, at 9 AM and 4 PM, and three times daily for the others, 9 AM, 12 noon, and 4 PM.

Administration of sex hormones began a few days after taking the first electroencephalograms, and was repeated daily, after recording the first EEG. We injected oily solutions of progesterone (Leningrad Chemical-Pharamaceutical Factory) in doses of 1 to 20 mg per diem, and oily solutions of folliculin (Ukrainian Institute of Experimental Endocrinology) in doses of 50 to 5,000 mouse units per diem. Some animals were first given folliculin, and then progesterone, while others received progesterone alone.

EXPERIMENTAL RESULTS

The most clear cut results were given by two rabbits, in the spring-summer season.

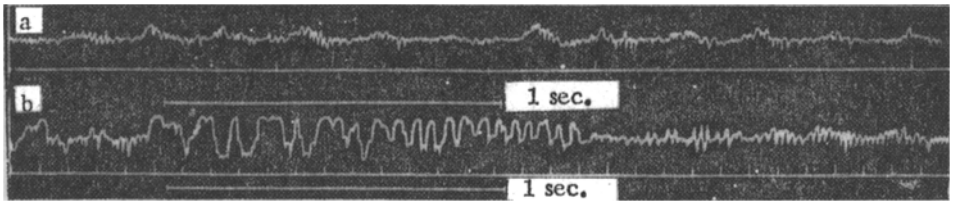

Fig. 1. Electroencephalogram of female rabbit No. 1. a) Background; b) 7 hours after injection of 1 mg of progesterone.

One of these rabbits received progesterone alone, at dosage levels of 1 mg daily for 3 days, 5 mg on the 4th, and 20 mg on the 5th day. The other doe was given folliculin: 50 International Units the first day, 200 I. U. the 2nd, 500 I. U. the 3rd, 1,000 I. U. the 4th, and 5,000 I. U. on the 5th day. Progesterone was given 4 days after the last injection of folliculin, in the same doses as for the first rabbit. The animals were castrated one month after the last injection of progesterone.

The EEG of the first rabbit, recorded before administration of progesterone, shows the presence of slow waves, of a frequency of 3-4 per second, and of fast waves, frequency 60-65 per second (Figure 1, a).

The first two injections of progesterone did not bring about any visible changes in the EEG.

Seven hours after the third injection of 1 mg of progesterone the EEG showed, in addition to the slow waves of frequency 3-4 per sec., and to the fast waves, frequency 60-65 per sec., sections of the tracing consisting of waves of a frequency of 10-15 per sec., of varying amplitude (Figure 1, b). These changes were no longer in evidence by the morning, the EEG being of the normal type. Similar slow waves of frequency 10-15 per sec. were again seen 7 hours after injecting 5 and 20 mg of progesterone. With increase in the dose of progesterone the number of sections showing these waves increased. These changes again disappeared by the next morning after the injections. After injecting 20 mg of progesterone behavioral changes also appeared in the animal: it refused food, avoided the other rabbits, and became much less active.

The EEG of the second rabbit, recorded before injection of hormones, shows the presence of slow waves, frequency 2-3 per sec., and fast waves, frequency 50-55 per sec (Figure 2, a).

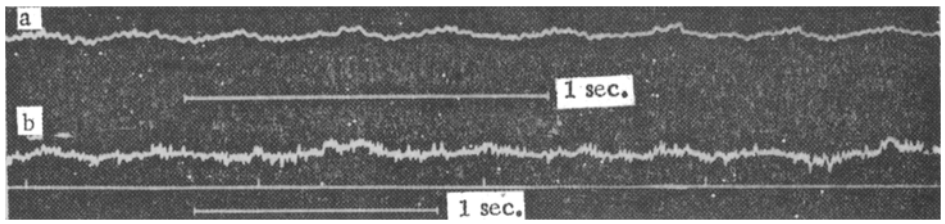

Fig. 2. Electroencephalogram of female rabbit No. 2. a) Background; b) 7 hours after injection of 500 I. U. of folliculin.

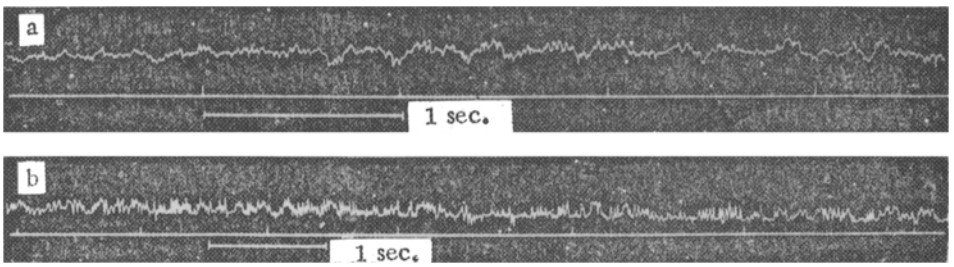

Fig. 3. Electroencephalogram of female rabbit No. 2. a) Before castration (1 month after the last progesterone injection); b) 12 days after castration.

Injection of 50 and 200 I. U. of folliculin on two successive days did not cause any evident changes in the EEG. Three hours after injection of 500 I. U. of folliculin there was still no change in the EEG, but 7 hours after injection of 500 I. U. of folliculin it was possible to observe an increase in the frequency of the fast waves, to 60-65 per sec. (Fig. 2, b). This effect was still in evidence on the following morning.

Injection of 1,000 I. U. of folliculin reduced the frequency of the fast waves to 50 per sec., and injection of 5,000 I. U. of folliculin on the following morning caused no further change in the EEG.

The EEG recorded 4 days after the last folliculin injection showed slow waves, frequency 2-3 per sec., and fast waves, frequency 52-55 per sec.

The first two injections of progesterone had no perceptible effect on the EEG. Three hours after the third 1 mg injection the EEG showed slow waves, frequency 10-15 per sec. The changes were similar to those seen after the third injection of progesterone into the previous rabbit.

Stretches of slow waves of frequency 10-15 per sec.could not be seen on the EEG until 48 hours after the 4th injection of 5 mg of progesterone, when this type of wave predominated.

The slow waves (10-15 cycles/sec.) were seen on the EEG recorded at 3 and 7 hours after injection of 20 mg of progesterone. The slow wave activity disappeared from the EEG as soon as the injections were discontinued. One month after the last injection of progesterone the EEG showed slow waves of a frequency of 3 per sec., and fast waves of a frequency of 50-55 per sec., i.e., the EEG had reverted to the initial pattern.

Castration was then performed, and this was followed by pronounced changes in the behavior of the rabbit.

Twelve days after castration clear-cut changes were evident in the EEG: the slow waves were absent, and waves of a frequency of 50-52 per sec. predominated, with a diversified amplitude (Figure 3, b).

Examination of the EEG for the two rabbits showed that the amplitudes of the waves in the morning recordings were smaller than for the evening ones.

The effects of folliculin and progesterone on the EEG of the other rabbits, which were recorded during the winter season, were much smaller, but in some of the experiments we found that administration of progesterone was followed by the appearance of slow waves of the same type as for the first two animals. The effect of folliculin was barely perceptible.

It thus appears that progesterone, whether administered after folliculin or before, caused the appearance of slow waves of a characteristic frequency. These waves appeared in two cases after administering 3 mg of progesterone over 3 days. The incidence of these slow waves increased with increasing doses of progesterone, and with diminution in the motor activities of the animals.

Doses of 750 I. U. of folliculin administered over 3 days caused an increase in the frequency of the waves. Further increase in the folliculin dosage to 5,000 I. U., led to a fall in the frequency, which did not, however, fall below the initial value.

Castration was followed by behavioral changes in the animals, and by disappearance of the slow waves, while the amplitude of the fast waves fluctuated widely throughout the recording.

Our experimental findings show that progesterone and folliculin exert different actions on the functional state of the cerebral cortex.

LITERATURE CITED

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[2] L. I. Shvang and I. Ya. Romm, Akusher. i Ginekol., 1953, No. 1, 25-32.