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CHANGES OF UTERUS MYOELECTRICAL ACTIVITY UNDER INFLUENCE OF SEROTONIN IN SHEEP SENSITISED AND NON-SENSITISED WITH STILBOESTROL

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ABSTRACT

The experiments were performed on 3 sheep which had bi-polar platinic electrodes subserously implanted to the uterus shank and horns during an operation. The registration of uterus myoelectrical activity was conducted by the use of Reega Duplex XVI electroencephalograph. The tests were carried out on sheep in uterus, sensitised and non-sensitised with Stilboestrol-Polfa (0.04 mg kg^{-1} i.m.). After recording the output uterus activity, the sheep were administered serotonin in continuous infusion in the quantity of: 12-24 µg kg^{-1} min^{-1}. The obtained results revealed that serotonin in sheep in anestrus, non-sensitised with stilboestrol, does not cause (within the scope of action potentials) any changes in the electrouterographic record. In sheep sensitised with stilboestrol, serotonin increases the uterus myoelectrical activity.

Key words: sheep, uterus, myoelectrical activity, serotonin

INTRODUCTION

Serotonin (5-hydroxytryptamine, 5HT) is a well-known mediator within the central nervous system. However, it is also present in the cells of many other systems of the organism. Its presence was proved in enterochromaphin cells of the stomach and small intestines as well as in intestine neurons (24). The occurrence of this amine was also discovered in uterus mast cells and in uterine tubes (15), in deferent ducts (4), ovaries and in uterine cervix (1). The demonstration of these data gave the beginning for research on the share of serotonin in controlling the alimentary tract and reproductive organ functions. The function of serotonin in the organism is complex, and the reason for it is the diversity of serotonin receptors located directly on smooth muscle cells, on nerve endings and within the central nervous system. The latest research proves that there are seven types of serotonin receptors (17,29). It has been discovered that serotonin, in various animal species, has a stimulating (10,16,26) or inhibiting (10,16,26) influence on the motor activity of particular sections of the alimentary tract. The investigations of serotonin influence on the motor activity of uterus smooth muscles in human and in various animal species reveal that also here there are differences in the direction of this amine's action. It was noted that serotonin stimulates the contractions of the uterus smooth muscles of a human being (18, 27), a rat (11,14), and a rabbit (28), yet in the pig's uterus it also causes the inhibiting by the $5HT_7$ receptors (17).

One of the ways enabling the controlling of uterus contraction dynamics in females and women is stimulating or blocking suitable molecular receptors. There are numerous kinds of these receptors in smooth muscles. Detailed knowledge of the role of each kind of receptors in the contraction control of uterus smooth muscles not only has a vital cognitive importance, but it can also be used in medical practice. The possibilities of controlling the uterus contraction dynamics in domestic animals depend on the knowledge of molecular receptor distribution, the receptors' thickness and the direction of their actions in particular species. They are also dependent on the broad recognition of all internal factors that may influence the reactivity of a given type of receptors. Some of these factors are hormones, particularly estrogens and progesterone. The reason for our initiating the experiments on the influence of serotonin on the uterus activity of smooth muscles in sheep was insufficient information on the share of serotonin in the controlling of the uterus motor function as well as demonstrating the inhibiting influence of this amine on the uterus motion function. The goal of this investigation was specifying the difference of myometrium sensitivity (reactivity) on serotonin in sheep non-sensitised and sensitised with stilboestrol in the myoelectrouterographic record.

MATERIALS AND METHODS

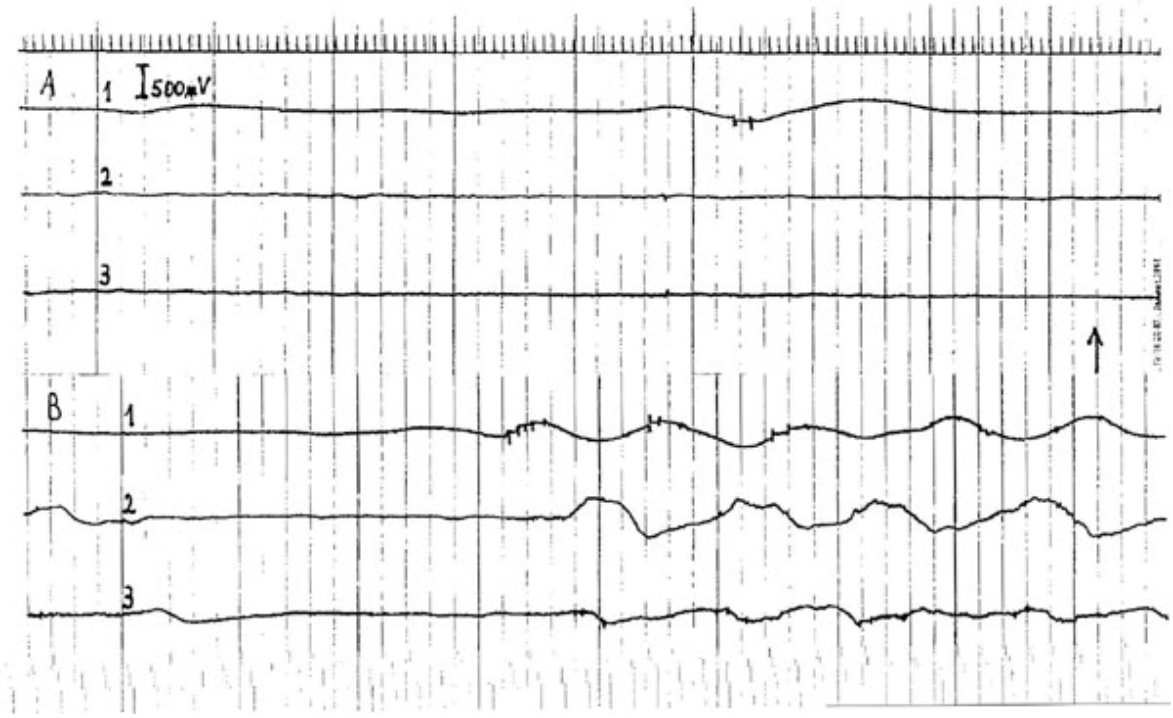
The experiments were carried out on 3 inter-breed hybrid ewes, aged from 12 to 50 months, having the body mass of 34, 40 and 52 kg. Before beginning the experiments, each sheep underwent an operation during which it had bi-polar platinic electrodes subserously implanted to the uterus shank and horns (23). The procedure was performed with general anesthesia, with the animal in its dorsal position. Cutting the skin and abdominal integument was conducted in the *linea alba* from the pubic symphysis to the navel. Then, after slight shifting of the horns and shank, the electrodes were implanted, positioned on plastic plates. After inserting the electrodes under the serosa, each plate was fastened with 4 nodule sutures to the uterus wall. Then, the electrode ducts were brought out outside through separate wholes in abdominal integuments. The abdominal cavity was sutured in layers. During 5 days after the operation the sheep were intramuscularly administered antibiotics and novaldin. The

experiments were launched two weeks after the operative procedure. The registration of the uterus myoelectrical activity was carried out by the use of Reega Duplex XVI electroencephalograph, with the time constant of 0.01s. The tests were performed on sheep in anestrus sensitised and non-sensitised with Stilboestrol-Polfa (0.04 mg kg^{-1} i.m.). Serotonin – serotonin creatynine sulphate (from the Sigma company) was intravenously administered in infusion through a catheter inserted into the external jugular vein, in the quantity of 12-24 µg kg^{-1} min^{-1}. Alltogether, 24 tests were carried out. The obtained electrouterograms were assessed by a visual method (12), confirmed by statistical analysis making use of t-Student test. The duration of breaks between the action potential cycles before and after administering 5HT were compared in this analysis.

RESULTS AND DISCUSSION

The records of biopotentials of the uterus horns and shank in sheep in anestrus non-sensitised with stilboestrol revealed a lack of action potentials during this time (Figure 1A). Other authors (20,21) achieved similar results. During this time the serotonin administered intravenously did not cause the formation of action potentials (Figure 1B). These results may indicate that serotonin inhibits the electrical activity of miometrium (which is not observed when the action potentials are absent) or that the concentration of serotonergic receptors in sheep in anestrus is too insignificant to cause the depolarization of uterus muscle cells. In earlier experiments we noted that in sheep in anestrus, the functional electrical activity of uterus does not change, either, after administering oxytocin (33), histamine (8), drugs stimulating the alpha-adrenergic receptors (7) and prostaglandin F_2alpha (9). In sheep sensitized with stilboestrol the cyclic myoelectrical activity was observed both in the uterus horns and shank.

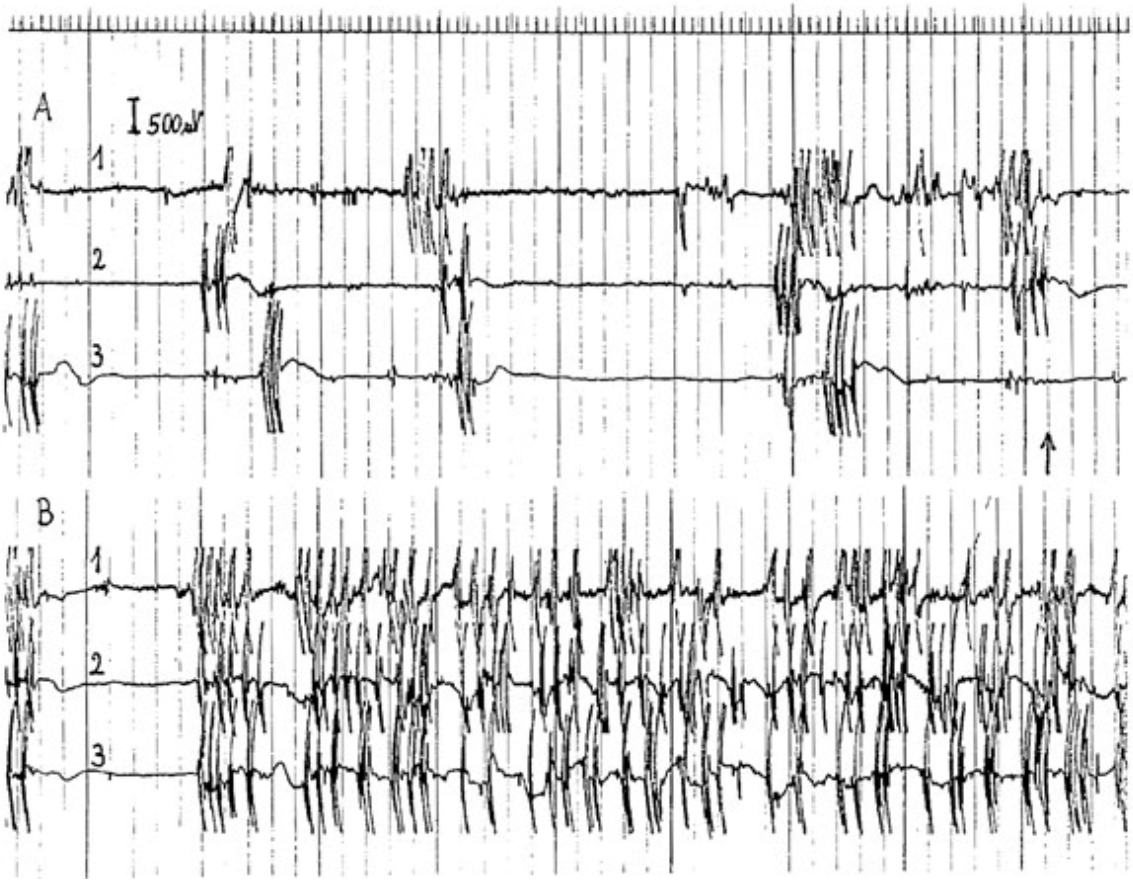
Figure 1. Lack of functional electrical activity in uterus in sheep in anestrus, non-sensitised with stilboestrol.



Notations: A – output record, B – record during serotonin infusion (arrow denotes beginning of infusion), records from: 1 – uterus shank, 2 – right horn, 3 – left horn, time (first record on top) - 1 sec.

The frequency of cycles (spindles) of action potentials in the second and third 24-hour period after sensitisation ranged from 2 to 4 per minute (Figure 2A). The intensity of this activity (amplitude and frequency of needle discharges) was the highest after the first and second 24-hour period from the sensitisation with stilboestrol, and then it decreased. The atrophy of action potentials in sheep occurred after 10th 24-hour period. In case of one sheep, this period was considerably prolonged. The results of one's own experiments stay in accordance with the data of other authors (20, 21, 25, and 32), who proved the stimulating influence of estrogens on uterus contractility. Yet, according to Lye and co-authors (19), 17beta-estradiol affects uterus contractility diphasically – first has an inhibiting, then a stimulating influence. In sensitised sheep, an intensified myoelectrical activity of uterus was recorded after the intravenous administration of serotonin (Figure 2B).

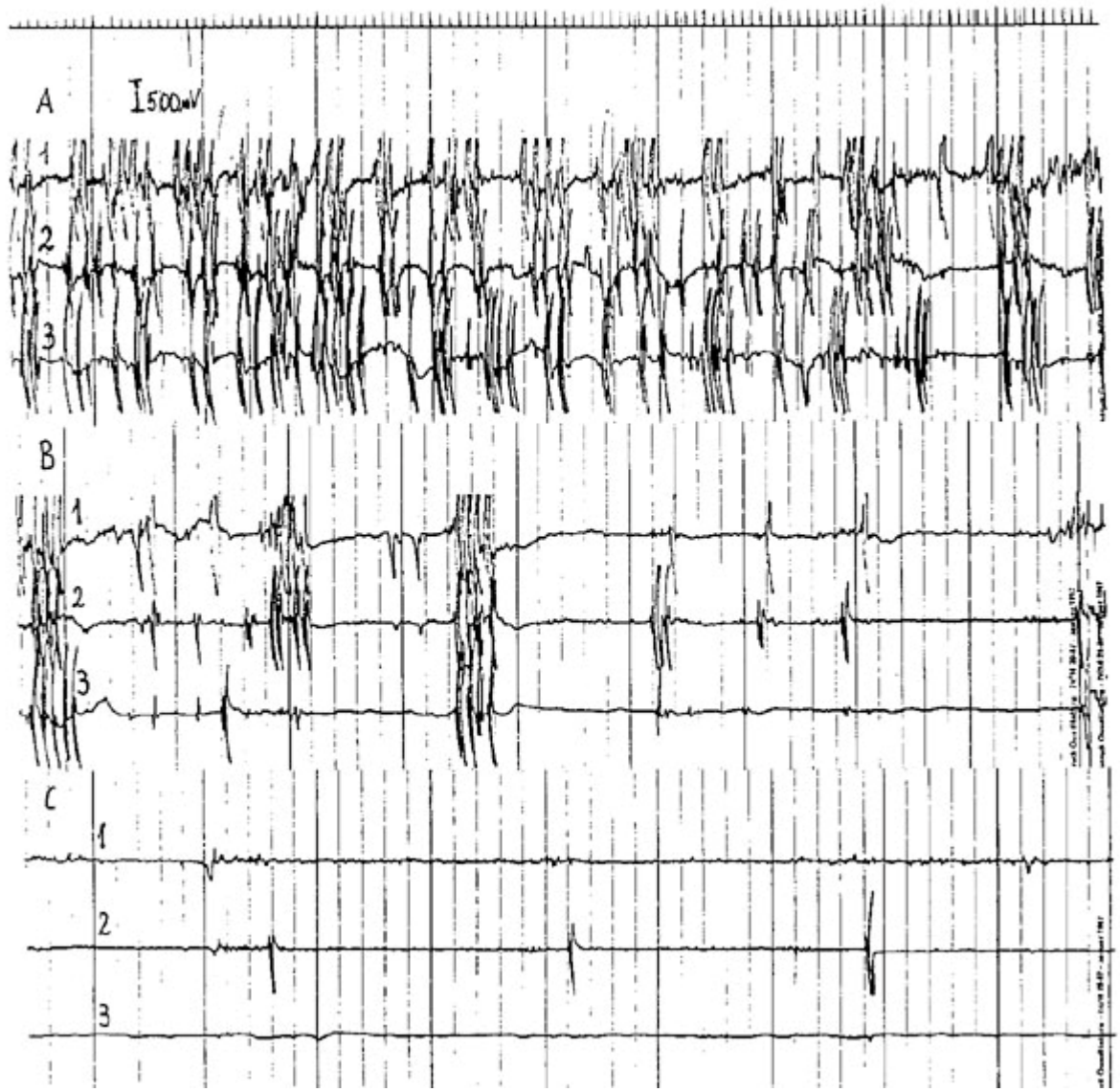
Figure 2. Uterus myoelectrical activity in sheep in anestrus after sensitisation with stilboestrol – before (A) and during serotonin infusion (B).



Notations as in figure 1.

The difference between the frequency of needle discharges before and after administering serotonin was statistically important (when p $\leq$0.01; t obl > stat). The disappearance of breaks between the cycles (spindles) of needle discharges was frequently noted. The sheep demonstrated the most intensive reaction to serotonin in the second and third 24-hour period after sensitisation with stilboestrol. After the activation of uterus myoelectrical activity caused by the administration of serotonin, a subsequent inhibition of this activity often took place (Figure 3).

Figure 3. Inhibiting of uterus myoelectrical activity in sheep after its activation caused by serotonin.



Notations: A – record after administration of serotonin, B – beginning of inhibiting, C – complete inhibiting. Remaining notations as in figure 1.

In our earlier sheep experiments, a similar reaction of inhibiting the myoelectrical activity after its activation was also revealed after the administration of oxytocin, histamine, adrenaline, PGF_2alpha, phenylephrine and dopamine (6). The conclusion of this part of the experiment is that the stimulation of 5HT receptors of sheep uterus causes the intensification of its myoelectrical activity, thus the obtained reaction direction is opposite to the one observed in pigs. As Kitazawa and co-authors noted, serotonin, in this species, inhibits the uterus contractions through $5Ht_7$ receptors. The demonstration of myometrium reactivity on serotonin in sheep complies with other authors' observations as late as after sensitisation with stilboestrol; the authors, using laboratory animals, discovered that the stimulating serotonin activity on uterus muscular coat depends on estrogens (3, 13, 14 and 28).

CONCLUSIONS

1. Serotonin does not cause any changes (within the range of action potentials) in the electrouterographic record in sheep in anestrus non-sensitised with stilboestrol.
2. Sensitsation of sheep in anestrus with stilboestrol causes myometrium sensitivity to serotonin.
3. Serotonin increases the uterus myoelectrical activity in sheep sensitised with stilboestrol.

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