ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://ijpp.com

Indian Journal of Physiology and Pharmacology

Short Communication

The role of oxytocin in the regulation of electrical activity of fallopian tubes in rats

Knarik Kazaryan[1], Naira Hunanyan[1], Margarita Danielyan[2], Arus Mkrtchyan[1], Roza Chibukchyan[1], Yulia Trofimova[1], Tatevik Piliposyan[1]

Departments of [1]Smooth Muscle Physiology and [2]Histochemistry and Morphology, L.A. Orbeli Institute of Physiology, Yerevan, Armenia.

***Corresponding author:**
Naira Hunanyan,
Department of Smooth Muscle Physiology, L. A. Orbeli Institute of Physiology, Yerevan, Armenia.

naira_hunanyan@yahoo.com

Received: 25 January 2024
Accepted: 18 August 2024
EPub Ahead of Print: 28 November 2024
Published: 27 December 2024

DOI
10.25259/IJPP_30_2024

Quick Response Code:

ABSTRACT

Objectives: The effect of oxytocin on spontaneous electrical activities of rhythmogenic areas in the right and left uterine horns (ovarian and cervical areas) was investigated in non-pregnant rats.

Materials and Methods: Comparative analysis of the main characteristics of spontaneous activity (amplitude of action potentials [A]; mean rise- rate [V]; rise - time [T/2]; half-width [t] of spikes; total duration of bursts in 1 minute [D], and spike generation frequency [F]) was conducted. Morphofunctional properties of the rat uterine horns were studied by using a histochemical method, which had been developed based on the Homori method.

Results: The left ovarian horn area is characterized by parameters significantly exceeding those of the other three areas, which are identical to each other. Administration of oxytocin, as a factor promoting increased excitability of the myometrium, led to significant enhancement of rhythmogenesis in the right ovarian horn area. Morphohistochemical results revealed an increase in enzymatic activity of the myometrium under the influence of oxytocin, with the right ovarian horn area showing the greatest changes.

Conclusion: Since oxytocin plays a key role in stimulating activity and enhancing the myometrial contractions of the right fallopian tube, the possibility of additional reserve capabilities in the regulation of the integrative function of the reproductive organs cannot be excluded from the study.

Keywords: Fallopian tubes, Ovarian horn area, Cervical horn area, Spontaneous activity, Oxytocin

INTRODUCTION

The reproductive system is a complex of organs (right and left fallopian tubes, uterine corpus and uterine cervix) that ensure the primary functional role of childbirth. Each of them has its own functional, autonomous activity.[1,2] This process is carried out by the propagation of peristaltic waves in the caudal direction, which is associated with pacemaker activity.[3,4] The latter is presented in the form of high-frequency spike-like action potentials, myogenic in nature, which are grouped into asynchronously arising and fading bursts of activity.

Unlike the uterine corpus, rhythmogenic areas of the fallopian tubes are localised in their. [terminal ends – ovarian and cervical horn areas.[5-8] At the same time, the ovarian horn area is the dominant pacemaker side, propagating electrical activity in the anterograde direction,[9] in contrast to the other horn areas, which allow to conduct of excitation waves in any orientation.[10,11]

The fallopian tubes are paired organs with identical physiological characteristics. At the same time, there is an asymmetry in relation to the parameters of rhythmogenesis in the ovarian

horn areas. [12] Certain reasons may contribute to this fact: Myogenicity, syncytial organisation of myometrium, specificity of innervation, humoral influence, etc.[1,13,14]

The muscular layer of the uterus (myometrium) is characterised by a special response to the hormone oxytocin, which is one of the main regulators of contractile activity during childbirth, by changing the patterns of excitation. Moreover, depending on the cell type, oxytocin receptors show variability in sensitivity. [13,15] The study of asymmetry among the electrophysiological characteristics of both ovarian horn areas will reveal the mutual regulation between the parameters of rhythmogenesis, ensuring consistent contractions. Characteristics of the effect of oxytocin on spontaneous activity will help to sort out this problem, which has been clarified by a combination of electrophysiological and morphofunctional studies.

MATERIALS AND METHODS

In vivo experiments were carried out on female rats weighing 200–250 g. Animals were anaesthetised by intraperitoneal injection of Nembutal (40–45 mg/kg). The peritoneal cavity was opened, and the uterine corpus with the uterine horns from two sides was exposed.

The uterus was denervated by transection of the nerves plexus hypogastricus, uterinus and uterovaginalis. [16] Oxytocin (5 IU/mL, Gedeon Richter, Hungary) loading dose 10^{-1} μg/kg was administered intravenously. Depending on the animal weight, such concentration was possible to administrate by different injection volumes – from 0.2 mL to 0.3 mL.

Registration of action potentials from smooth muscles of the right and left fallopian tubes was performed simultaneously from the surface of ovarian and cervical areas. Bipolar silver electrodes with a diameter of 0.5 mm were used. The distance between electrodes was 3 mm, and the resistance of the muscle tissue between the electrodes reached 100–120 kOhm. The potential difference formed among the electrodes was transmitted to a specially developed four-channel electronic device, which provided amplification and digitisation of the incoming signals. The digitised signals were then transmitted to a computer for visualisation, storage and subsequent analysis. The signal registration program was developed using the National Instruments Lab View Biomedical Toolkit. It should also be noted that the developed device ensures reliable recording of changes in electrical signals between different areas of muscle tissue with an accuracy of up to 5 μV.

The analysis of the results was carried out by determining values of the main parameters of spontaneous action potentials: A – amplitude, V – mean rise-rate, T/2 – rise-time (action potential duration of upgoing phase) and t – half-width (action potential duration forming the upper half of its amplitude) of spikes, as well as D – total duration of bursts in 1 min and F – spike generation frequency.

The subsequent statistical analysis of recorded signals was carried out using the Origin-8.5 and Sigma Plot 11.0 software. Student's *t*-test was used to calculate the standard error of the difference between the means and determine statistically significant changes.

To study the morphofunctional properties of the rat uterine horns, a histochemical method was used to detect calcium ions (Ca^{2+})-dependent acid phosphatase activity, [17] which had been developed based on the Homori method. After anaesthesia, the uterine horns were removed and fixed in the 5% neutral formalin solution. Frozen sections were transferred to freshly prepared incubation mixtures to detect Ca^{2+}-dependent acid phosphatase activity. The obtained specimens were examined under an OPTON light microscope (West Germany), and micrographs were taken using the AmScope MU 800 camera.

RESULTS

Simultaneous registration of bursting electrical activity from the rhythmogenic areas of both uterine horns was done. According to the results shown in Table 1, the parameters of their action potentials have certain differences. Moreover, the largest values of the main activity characteristics were recorded in the left ovarian horn area.

In contrast to that, definite similarities have been shown between activity characteristics of the other three loci of uterine tubes. Figure 1A presents a typical picture of rhythmogenesis in one of such loci (2) and in the left ovarian horn area (1). On the right, the averaged unfolded spike forms are shown.

The effect of oxytocin on the spontaneous activity of the horns was revealed by its injection into the femoral vein of the animal in 0.2–0.3 mL volume. Our previous studies have shown that the loading dose of oxytocin 10^{-1} μg/kg is optimal for stimulating myometrium.[18] Comparative analysis of the rhythmogenesis in the left and right ovarian horn areas, under the effect of oxytocin, has revealed a significant increase in action potential parameters of the right ovarian horn area [Figure 1b]. The results were calculated in percentage ratio to the norm (taken as 100%). According to the Figure 1b, there is a simultaneous increase in the values of A, T/2 and D, respectively, by 59.8%, 60.8% and 56.3%. The frequency of spikes (F) increased more than 3 times compared to the norm. Unlike these results, oxytocin has a different effect on the activity of the cervical horn areas. As shown in Table 1, there are similarities between their activity parameters in the norm, and correspondingly, this hormone affects them in the same manner [Figure 1C].

Table 1: Activity parameters of action potentials in the ovarian and cervical horn areas in norm.

Registration areas and number of experiments, *n*		Amplitude of action potentials (A), μV	Mean rise-rate of spikes (V), μV/sec	Rise-time of spikes (T/2), sec	Half-width of spikes (t), sec	Spike generation frequency (F), Hz	Duration of bursts in minute (D), min
Ovarian horn	Left	84.54±3.92	1121.10±1.10	0.08±0.00	0.06±0.00	1.28±0.09	0.64±0.01
area, *n*=10	Right	57.07±0.28	767.68±6.65	0.06±0.00	0.07±0.00	1.23±0.07	0.54±0.03
Cervical horn	Left	55.53±0.84	621.77±2.20	0.08±0.00	0.06±0.00	1.18±0.07	0.54±0.02
area, *n*=10	Right	56.61±0.23	620.77±0.63	0.07±0.00	0.06±0.00	1.13±0.08	0.53±0.03

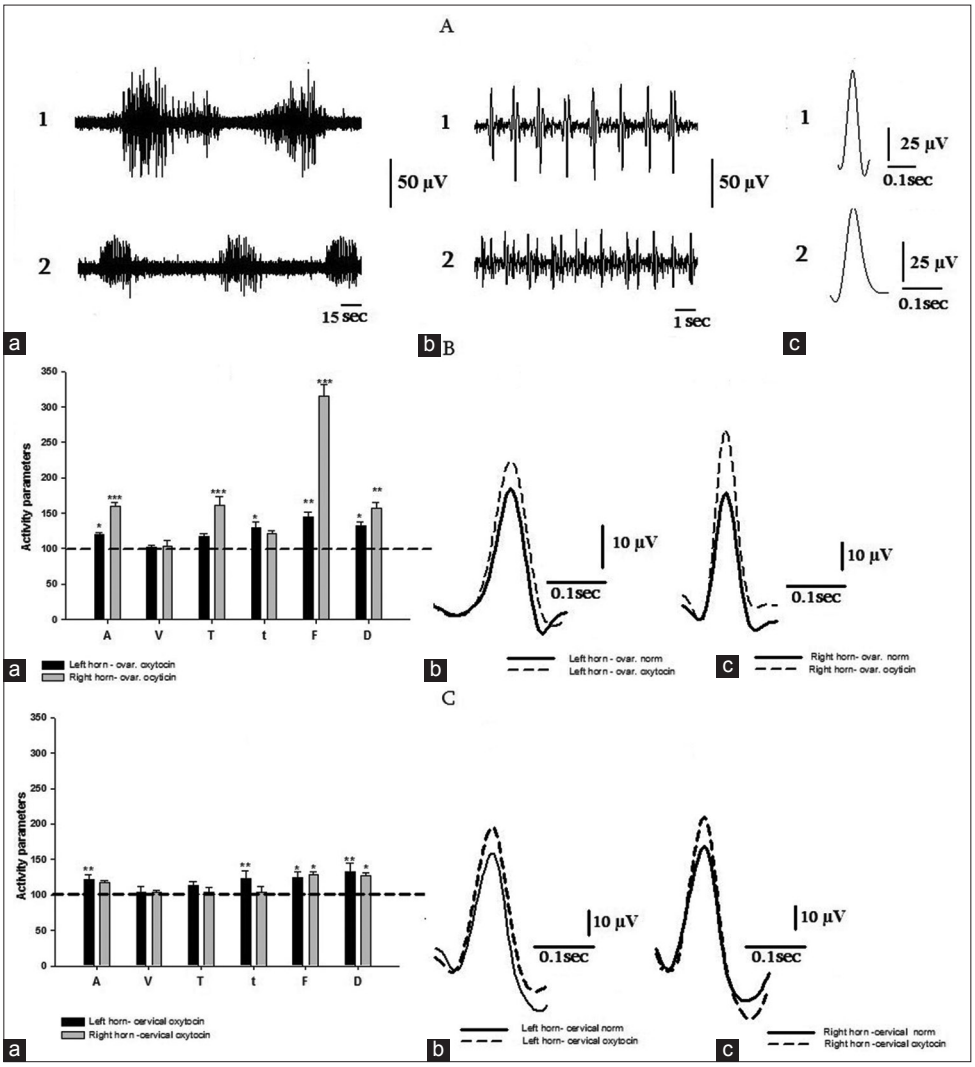

Figure 1: (A) a. Bursts of spikes in the ovarian (1) and cervical (2) areas of the left uterine horn. b. Following each other action potentials, recorded in bursts of the left ovarian and cervical horn areas. c. Averaged forms of action potentials in the corresponding areas. (B) a. The effect of oxytocin on spontaneous electrical activity of the ovarian areas in relation to the norm (dashed line). b. and c. Superimposed on each other, the averaged action potential contours in norm and under the effect of oxytocin. (C) a. The effect of oxytocin on spontaneous electrical activity of the cervical areas in relation to the norm (dashed line). b. and c. Superimposed on each other, the averaged action potential contours in norm and under the effect of oxytocin.

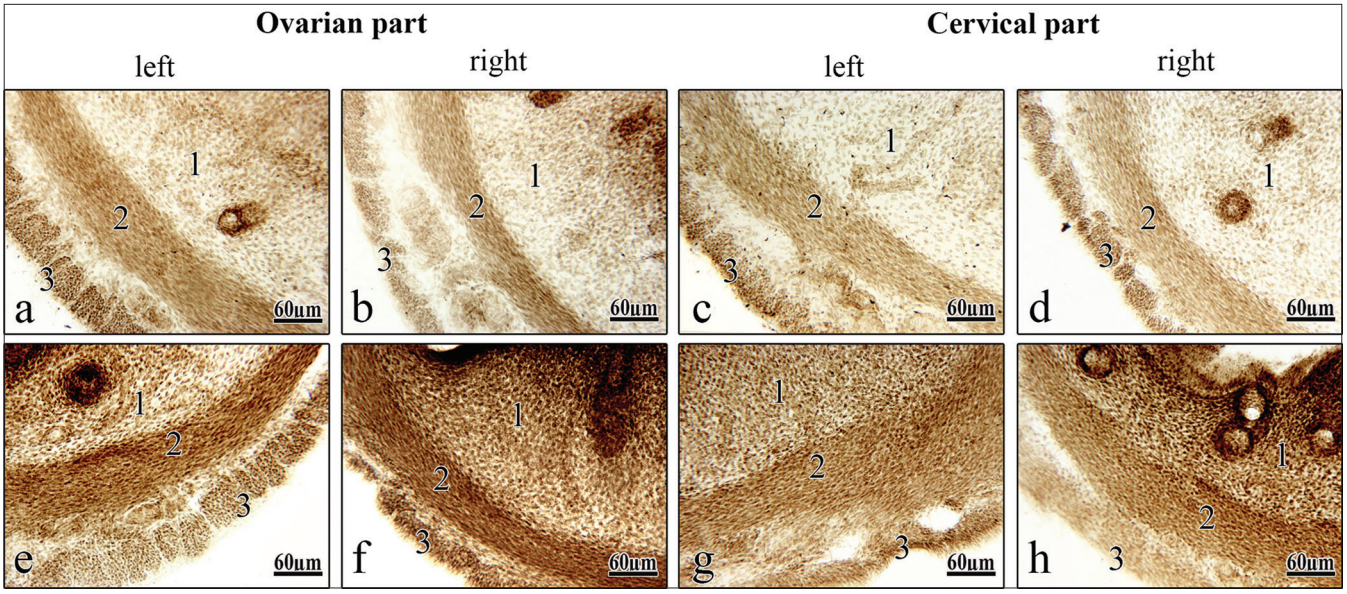

Figure 2: Figure 2: Frontal sections of the rat uterine horns (a-d)- in norm and (e-h)- under the effect of oxytocin , 1 – mucous membrane; 2 – muscular layer; 3 – serous membrane. (a, b, e, f) – ovarian horn area; (c, d, g, h) - cervical horn area; (a, c, e, g) – left uterine horn; (b, d, f, h) – right uterine horn. Magnification: 160 X (a-h), digital magnification: 8MP.

Histological sections revealed all three layers of the fallopian tubes. There were no significant differences in the staining intensity of mucous and serous membranes in the different horn areas [Figure 2a-h]. However, the metabolism of myogenic elements showed considerable differences in the myometrium, and the right and left horns of the uterus reacted differently in the norm and under the effect of oxytocin [Figure 2a-h]. In intact animals, myogenic structures of the left ovarian horn area were stained most intensely, indicating the high level of metabolic processes [Figure 2a]. Meanwhile, myogenic structures in the right ovarian and both cervical horn areas were stained relatively equally and moderately [Figure 2b-d].

Under the effect of oxytocin, there is an increase in the activity (increase of metabolism) of smooth muscle cells along the right and left horns of the uterus [Figure 2e-h] compared to intact animals [Figure 2a-d]. At the same time, myogenic cells are no longer represented as separate units but in the form of cytoplasmic mass with multiple nuclei as these cells merge. The activity of acid phosphatase increases sharply, and cytoplasmic granulation cannot be distinguished. The highest enzymatic activity was noticed in the right ovarian horn area [Figure 2f], in comparison to the left ovarian and both cervical areas of the uterine horns [Figure 2e, g, h].

DISCUSSION

Oxytocin promoted specific, sharp changes in rhythmogenesis of the right ovarian horn area. The results of morphohistochemical studies confirmed the obtained electrophysiological results: oxytocin increased enzyme activity in the myometrium of all rhythmogenic areas of the rat uterine both horns, but the highest increase in activity has been shown for the right ovarian horn area. Based on the analysis of morphofunctional states of different uterine horn areas, it can be assumed that the changes in the peristaltic velocity are based on the features of myogenic automatism in myometrium.

CONCLUSION

Due to the high electrophysiological activity, the left fallopian tube generates strong myometrial contractions in norm, compared to the right horn. However, since oxytocin plays a fundamental role in the activity stimulating process, administration of this hormone sufficiently enhances rhythmogenesis in the right ovarian horn area. Thus, this fact may indicate that there are some reserve possibilities for realization of the main role of the reproductive organ.

Ethical approval

The experimental protocol corresponded to the conditions of the European Communities Council Directive (2010/63/UE) and was approved by the Ethics Committee of Yerevan State Medical University after Mkhitar Heratsi (IRB Approval N4, November 15, 2018).

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

Financial support and sponsorship

This study has been completely performed by budget money of the L.A. Orbeli Institute of Physiology, NAS of Armenia, Yerevan. An additional financial support wasn't received for the realization of this project.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Domino M, Pawlinski B, Gajewska M, Jasinski T, Sady M, Gajewski Z. Uterine EMG activity in the non-pregnant sow during estrous cycle. J BMC Vet Res 2018;14:176.
2. Mancinelli R, Guariglia L, Racanicchi C, Bertuzzi A, Salinari S, Vitelli R. *In vitro* motility of non-pregnant rat uterine horns. Q J Exp Physiol 1988;73:459-69.
3. Garfield RE, Maner WL. Physiology and electrical activity of uterine contractions. J Semin Cell Dev Biol 2007;18:289-95.
4. Aguilar HN, Mitchell BF. Physiological pathways and molecular mechanisms regulating uterine contractility. J Hum Reprod Update 2010;16:725-44.
5. Parkington HC, Coleman HA. Excitability in uterine smooth muscle. J Front Horm Res 2001;27:179-200.
6. Maner WL, Saade GR, Garfield RE. The physiology of uterine contractions. J Clin Perinatol 2003;30:665-76.
7. Hutchings G, Williams O, Cretoiu D, Ciontea SM. Myometrial interstitial cells and the coordination of myometrial contractility. J Cell Mol Med 2009;13:4268-82.
8. Rabotti C, Mischi M. Propagation of electrical activity in uterine muscle during pregnancy. J Acta Physiol (Oxf) 2015;213:406-16.
9. Kelsi ND, Travis L, Elizabeth AH, Nick JS. Identification of a novel distension-evoked motility pattern in the mouse uterus. Am J Physiol 2021;321:R317-27.
10. Dodds KN, Staikopoulos V, Beckett EA. Uterine contractility in the nonpregnant mouse: Changes during the estrous cycle and effects of chloride channel blockade. J Biol Reprod 2015;92:141.
11. Lammers WJ, Stephen B, Al-Sultan MA, Subramanya SB, Blanks AM. The location of pacemakers in the uteri of pregnant guinea pigs and rats. Am J Physiol Regul Integr Comp Physiol 2015;309:R1439-46.
12. Kazaryan KV, Hunanyan NG, Mkrtchyan AV. Spontaneous electrical activity of the rat fallopian tubes. J Evol Biochem Physiol 2020;56:245-50. (in Russian).
13. Shmygol A, Gullam J, Blanks A, Thornton S. Multiple mechanisms involved in oxytocin-induced modulation of myometrial contractility. J Acta Pharmacol Sin 2006;27:827-32.
14. Kazaryan KV, Hunanyan NG, Mkrtchyan AV. Comparative analysis of the electrophysiological properties of the rat fallopian tubes. EESJ 2019;45:11-5. (in Russian).
15. Kimura T, Takemura M, Nomura S, Nobunaga T, Kubota Y, Inoue T. Expression of oxytocin receptor in human pregnant myometrium. Endocrinology 1996;137:780-5.
16. Chuhrienko DP, Lyutko AV, Romanenko NT. Atlas of urogynecologic surgeries (female genitourinary system) surgery. Kiev: Visha Shkola; 1981. (In Russian).
17. Meliksetyan IB. Detection of Ca^{2+}-dependent acid phosphatase activity in the cellular structures of the rat brain. Morphology 2007;131:77-80 (in Russian).
18. Kazaryan KV, Hunanyan NG, Meliksetyan IB, Hakobyan RR, Savayan AA. Role of oxytocin in activation of spontaneous electrical activity of uterine corpus and uterine tubes in non-pregnant rats. J Evol Biochem Physiol 2011;47:284-91.

How to cite this article: Kazaryan K, Hunanyan N, Danielyan M, Mkrtchyan A, Chibukchyan R, Trofimova Y, *et al*. The role of oxytocin in the regulation of electrical activity of fallopian tubes in rats. Indian J Physiol Pharmacol. 2024;68:335-9. doi: 10.25259/IJPP_30_2024