GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 11 (368) ноябрь 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
NO 11 (368) 2025

Содержание:

GEORGIAN MEDICAL NEWS
No 11 (368) 2025

OXYTOCIN-MEDIATED COORDINATION OF RHYTHMOGENIC ACTIVITY IN THE MYOMETRIUM

Knarik V. Kazaryan[1], Naira G. Hunanyan[2,3]*, Tatevik A. Piliposyan[4,5], Margarita H. Danielyan[6], Arusyak V. Mkrtchyan[7], Harutyun Yu. Stepanyan[8], Hermine Kh. Mkrtchyan[9], Rosa G. Chibukchyan[4,10].

[1]*Laboratory Head of Smooth Muscle Physiology, 22 Orbeli Bros. str. 0028, Orbeli Institute of Physiology, Yerevan, Armenia.*

[2]*Senior Researcher at Laboratory of Smooth Muscle Physiology, 22 Orbeli Bros. str. 0028, Orbeli Institute of Physiology, Yerevan, Armenia.*

[3]*Senior Lecturer at University of Traditional Medicine, 38a Marshal Babajanyan St, Yerevan, Armenia.*

[4]*Researcher at Laboratory of Smooth Muscle Physiology, 22 Orbeli Bros. str. 0028, Orbeli Institute of Physiology, Yerevan, Armenia.*

[5]*Lecturer at Yerevan Haybusak University, 6 Abelyan St., Yerevan, Armenia.*

[6]*Laboratory Head of Histochemistry and Morphology, 22 Orbeli Bros. str. 0028, Orbeli Institute of Physiology, Yerevan, Armenia.*

[7]*Junior Researcher at Laboratory of Smooth Muscle Physiology, 22 Orbeli Bros. str. 0028, Orbeli Institute of Physiology, Yerevan, Armenia.*

[8]*Researcher at Laboratory of Central Nervous System functions compensation Physiology, 22 Orbeli Bros. str. 0028, Orbeli Institute of Physiology, Yerevan, Armenia.*

[9]*Assistant at Laboratory of Smooth Muscle Physiology, 22 Orbeli Bros. str. 0028, Orbeli Institute of Physiology, Yerevan, Armenia.*

[10]*Department Head of Medical Science, Lecturer at the Yerevan Gladzor University, Surb Grigor Lusavorich St., 7/1 Building, Yerevan, Armenia.*

Abstract.

The characteristics of spontaneous electrical activity forming bursts of action potentials in the main rhythmogenic areas of the myometrium (ovarian area, cervical area, uterine corpus) were investigated. The results were analyzed by determining the values of the following parameters of action potentials: amplitude (A), mean rise-rate (V), rise-time (T/2), and half-width (t). The obtained data indicate that the ovarian horn area represents a distinct rhythmogenic site, characterized by generation of bursts of discharges with properties unique to this area, in contrast to the activity patterns observed in the cervical horn area and uterine corpus.

Oxytocin, through its excitatory action, induces a synchronous increase in the measured parameters across the studied areas to the same extent. Comparable alterations in the main activity characteristics were observed under conditions of complete isolation of each uterine horn locus. Administration of oxytocin following isolation of loci resulted in a marked increase in spike amplitude and rise rate of action potentials in the ovarian area, approaching values observed in norm. Thus, these findings indicate that the ovarian horn area serves as a leading rhythmogenic site. Morphochemical results demonstrated the presence of different "functional" states in the examined myometrial areas, which is consistent with the presented electrophysiological data.

Key words. Ovarian horn area, spontaneous activity, transection, oxytocin, coordination of rhythmogenesis.

Introduction.

Among the visceral organs, the uterus is of particular importance due to its specific physiological role - regulating the contractile activity of the uterine corpus and fallopian tubes for the implementation of various reproductive functions, foremost of which is childbirth. This process is provided by the spontaneous electrical activity of the myometrium, whose cells behave as a functional syncytium [1,2].

The propagation of electrical activity is represented by successively grouped bursts of spike-like action potentials [2,3]. This form of spontaneous activity ensures the emergence of contractility, a fundamental determinant of myometrial function [3-5]. However, in norm, the propagation of the excitation wave is not observed, and this rhythmogenesis is shown only for the uterine corpus and local areas of the myometrium (the ovarian and cervical zones of the horns) [6,7]. Moreover, the propagation of a polarity-directed excitation wave is ensured by the ovarian horn area, which has been identified as a key rhythmogenic locus of the uterus [8,9].

All rhythmogenic regions of the uterine horns and the uterine corpus, while inherently myogenic and automatic, are modulated by humoral factors [10,11]. Among these, the hypothalamic neuropeptide released by the posterior pituitary, oxytocin plays a central role in regulating contractile activity [2,12,13]. Its excitatory effect, reflected in an increased frequency of spike discharges, may contribute to processes that ensure the integrative activity of all rhythmogenic areas in the myometrium. Investigating the electrophysiological properties of these regions provides important insights into the mechanisms that ensure their coordination for the implementation of the main contracture activity. The present work aimed to address the above-mentioned questions through an integrated approach combining electrophysiological and morphofunctional studies, alongside a comparative evaluation of activity parameters.

Materials and Methods.

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

The uterus was denervated by transection of the nerves plexus hypogastricus, uterinus, uterovaginalis. Oxytocin (5 IU/ ml, Gedeon Richter, Hungary) loading dose 0.1 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.

Action potentials from the smooth muscles of the uterine tubes and uterine corpus were recorded simultaneously from the surface of the corresponding 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 eight-channel electronic device, which provided amplification and digitisation of the incoming signals [14]. 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 by using Origin-8.5 and Sigma Plot 11.0 softwares. Statistical comparisons between two groups were performed using paired t-tests, while differences among more than two groups were analyzed using one-way ANOVA followed by appropriate post-hoc tests.

Histochemical study:

To investigate the morphofunctional properties of the rat uterine horns and corpus, a histochemical method was used to detect Ca^{2+}- dependent acid phosphatase (AP) activity [15,16], which had been developed on the basis of the Homori method. Euthanasia of intact animals was performed using Nembutal (100 mg/kg, intraperitoneally). Experimental animals receiving oxytocin were first anesthetized with Nembutal (40–45 mg/kg, intraperitoneally), followed by hormone administration. Five minutes later, additional Nembutal was administered for euthanasia. The extracted uterus was fixed in a 5% neutral formalin solution for 48 hours at +4°C. Sections of the relevant uterine areas were made in the frontal plane. Frozen sections, with a thickness of 30-40 μm, were transferred to freshly prepared incubation mixtures designed to detect the activity of Ca^{2+}- dependent AP. The obtained specimens were examined under an OPTON light microscope (West Germany), micrographs were taken by using AmScope MU 800 camera.

Methodological procedure:

Following rinsing in distilled water, tissue sections were immersed in a freshly prepared incubation medium composed of 20 ml of 0.4% lead acetate solution, 5 ml of 1 M acetate buffer (pH 5.6), and 5 ml of 2% sodium β-glycerophosphate solution. The mixture was adjusted to a final volume of 100 ml with 3% calcium chloride solution (anhydrous), filtered, and used for incubation. Sections were incubated at 37 °C for 1.5–3 h, subsequently rinsed in distilled water, treated with sodium sulfide solution for visualization, rinsed again, and finally mounted in balsam.

The histochemical method employed in this study enables the assessment of the activity of the examined structures, as it relies on the histochemical principle of identifying chemically active groups within the tissue—in this case, Ca^{2+}-dependent acid phosphatase activity. The method applied fully satisfies the requirements of this principle. In living organisms, enzymes serve as biocatalysts that facilitate the progression of metabolic reactions due to the presence of active centers that convert a substrate specific to each enzyme [17]. This methodological approach is based on the detection of intracellular phosphorus-containing compounds that play key roles in the energetic processes aimed at preserving and reproducing vital systems. This methodological approach, in addition to its histochemical significance, is of certain morphological interest. The obtained image is adequate, highly informative, and provides insight into specific metabolic pathways of the examined structures.

All procedures involving animals were carried out in accordance with the rules of the European convention for the protection of vertebrate animals used for experimental and other scientific purposes (Directive 2010/63/EU).

Results and Discussion.

Simultaneous recording of electrical activity allows the registration of bursts of action potential discharges from three autonomous rhythmogenic areas of the myometrium (Figure 1). These periodically occurring bursts of activity discharges function independently and asynchronously, differing from one another in their characteristics [13,18].

Analysis of the main characteristics of action potentials forming bursts in each of the rhythmogenic areas under normal conditions revealed distinct differences in their properties. As shown in Table 1, the ovarian horn area is characterized by high-amplitude spikes that markedly exceed those observed in the caudally located cervical horn area and the uterine corpus.

For clarity of analysis, all results are presented as percentages relative to the action potential parameters of the ovarian horn area, which was taken as the control - 100% (Figure 2).

As shown in the figure, activity parameters differ between areas: spike amplitude and mean rise-rate are markedly higher in the ovarian horn area, whereas spike rise-time is more than threefold and half-width is more than twofold lower compared with the cervical horn area and uterine corpus.

The data obtained in this study indicate a somewhat distinct pattern of activity in the ovarian horn area, which generates characteristic bursts of discharges that differ from those observed in the more caudally areas of the myometrium. The revealed differences in the parameters of action potentials forming activity bursts in the ovarian, cervical horn areas and uterine corpus may underlie corresponding variations in the properties of the bursts themselves. At the same time, although bursts originating in these regions do not occur simultaneously, their synchronized activity within certain time intervals cannot be excluded (Figure 1B). The highest spike amplitude and rise - rate were observed in the ovarian horn area of the myometrium, with these parameters gradually decreasing in the cervical horn area and the uterine corpus.

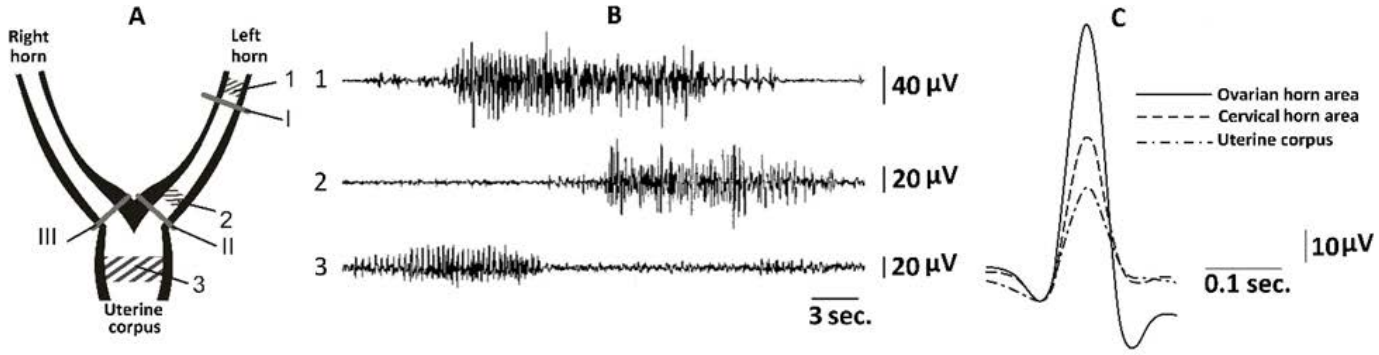

Figure 1. *A. Schematic representation of the rat uterine corpus and uterine tubes showing the sites of activity registration from the ovarian (1), cervical (2) areas of the left uterine tube, and the uterine corpus (3). Sites of uterine tube transections are indicated as I–III. B. Representative bursts of electrical activity recorded from areas 1–3 of the myometrium. C. Overlay of averaged action potential waveforms obtained from activity bursts in regions 1–3 (n = 14).*

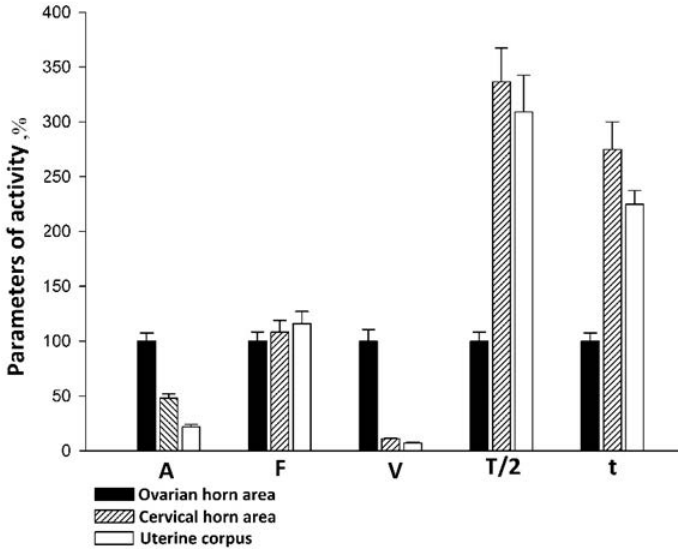

Figure 2. *Percentage values of action potential parameters from different areas of the myometrium relative to the ovarian area (n = 14).*

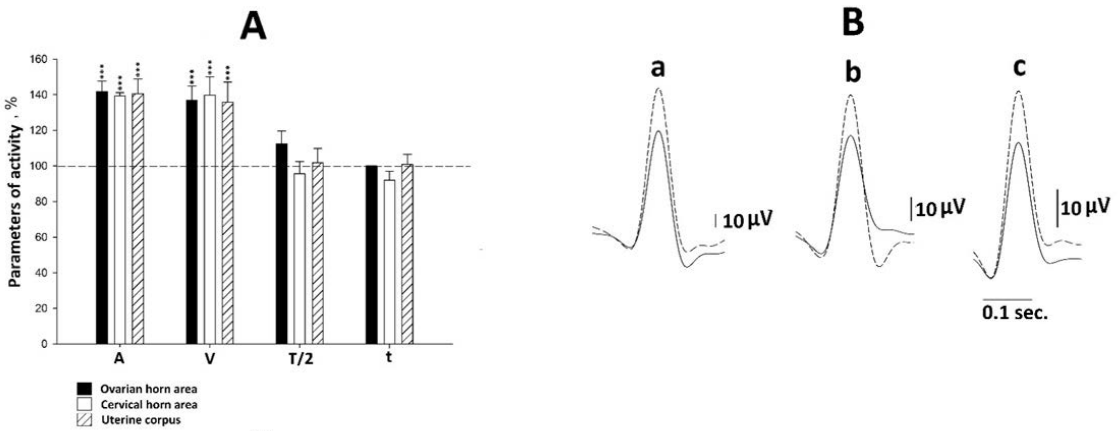

Figure 3. *Effect of oxytocin on the spontaneous electrical activity of regions 1, 2, and 3 (see Figure 1). A — Percentage ratios of action potential parameters after oxytocin administration in relation to the norm. The dashed line indicates the norm (baseline level, 100%). Statistical comparisons were performed using paired t-tests; ***P < 0.001. B (a) — Superimposed averaged waveforms of action potentials recorded from the ovarian horn area in norm (solid line) and under oxytocin exposure (dashed line). B (b) — Same as in panel "B (a)" for the cervical horn area. B (c) — Same as in panel "B (a)" for the uterine corpus. n = 14.*

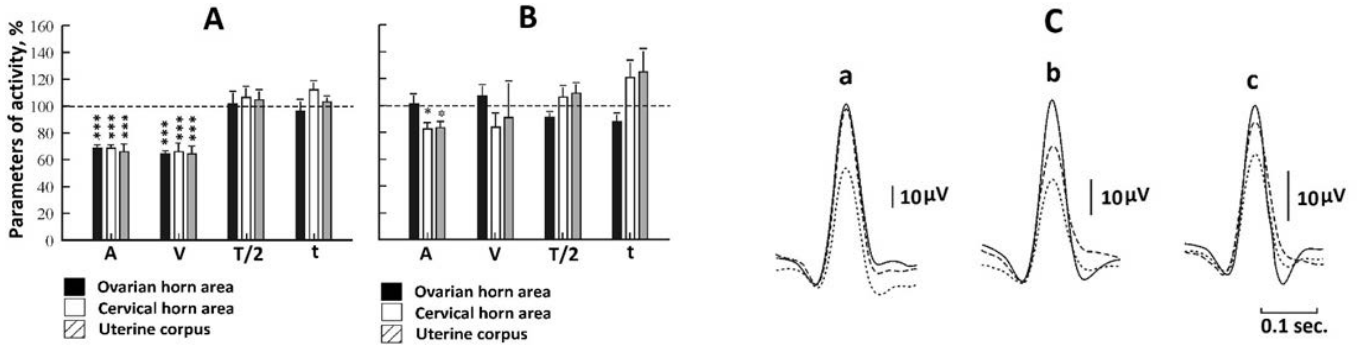

Figure 4. *Effect of oxytocin on spontaneous electrical activity after disruption of interconnections between rhythmogenic areas. A — Percentage ratios of action potential parameters relative to norm (prior to transection, baseline level, 100%) following isolation of the regions. B — Percentage ratios of action potential parameters relative to norm (prior to transection, baseline level, 100%) following oxytocin administration in isolated areas. For panels A and B, the dashed line indicates the baseline (100%). Statistical comparisons were performed using paired t-tests; *p<0,05, ***p < 0.001. C(a) — Superimposed averaged waveforms of action potentials recorded from the ovarian horn area in norm (solid line), after isolation (dash-dotted line), and following oxytocin administration (dashed line). C(b) — Same as in panel "C(a)" for the cervical horn area. C(c) — Same as in panel "C(a)" for the uterine corpus. n = 14.*

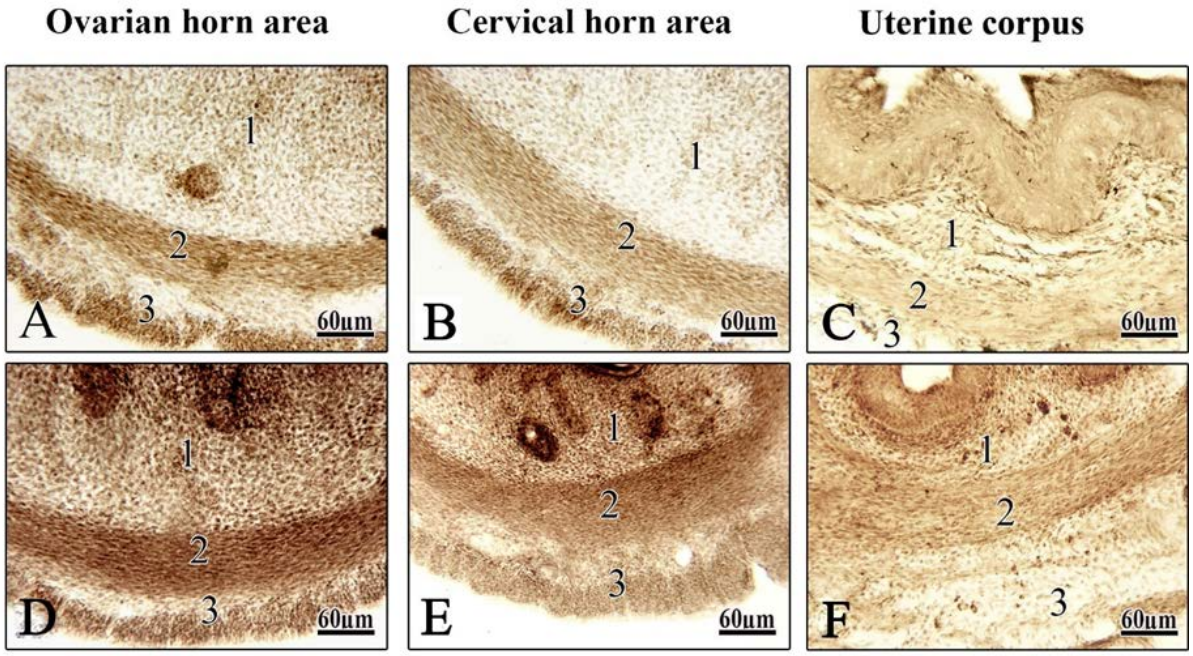

Figure 5. *Frontal sections of the rat uterus in norm (A-C) and under the effect of oxytocin (D-F): A, D - ovarian horn area; B, E- cervical horn area; C, F - uterine corpus; 1 - inner layer, 2 - middle layer, and 3 - outer layer of the myometrium. Electrophysiological recordings were obtained using surface electrodes and reflect the activity of the entire muscle layer. Magnification: 160x (A-F), digital magnification - 8MP.*

Table 1. *Parameters of spontaneous action potentials in different areas of the rat myometrium in norm. (M ± SEM).*

Registration areas and number of experiments, n	**Amplitude of action potentials (A), µV**	**Mean rise-rate of spikes (V), µV/sec**	**Half-width of spikes (t), sec**	**Rise-time of spikes (T/2), sec**
Ovarian horn area (1), n =14	86,02±1,71	1747,86±32,72	0,04±0,00	0,05±0,00
Cervical horn area (2), n =14	50,40±1,32	1023,29±28,29	0,04±0,00	0,05±0,00
Uterine corpus (3), n =14	33,42±1,40	836,39±29,55	0,04±0,00	0,04±0,00

Table 1.1. *One-way ANOVA summary for amplitude, rise-rate, and rise-time across myometrial regions. Amplitude differed significantly among regions (F(2,39)=327.86, P<0.001; normality P=0.283; homogeneity P=0.651), with post-hoc Holm–Sidak tests showing differences between all areas. Rise-rate also showed a significant regional effect (F(2,39)=253.43, P<0.001; normality P=0.120; homogeneity P=0.584), with all pairwise differences significant (confirmed by Post-hoc Holm–Sidak tests). Half-width differed among regions (F(2,39)=19.31, P<0.001; normality P=0.598; homogeneity P=0.921); uterine corpus and cervical horn area values were longer than ovarian horn area (P<0.001), with no difference between uterine corpus and cervical horn area (P=0.902) (confirmed by Post-hoc Holm–Sidak tests). A Kruskal–Wallis test for rise-time (H(2)=28.40, P<0.001; normality P=0.201; homogeneity P<0.05) confirmed shorter uterine corpus T/2 than ovarian and cervical horn area (P<0.05), while ovarian and cervical did not differ (P>0.05) (Post-hoc Tukey pairwise comparisons). *P<0,05, ***P < 0.001.*

Statistical Comparison of Myometrial Regions	**Amplitude of action potentials (A), µV**	**Mean rise-rate of spikes (V), µV/sec**	**Half-width of spikes (t), sec**	**Rise-time of spikes (T/2), sec**
	Mean difference			**Difference of Ranks**
Ovarian horn area vs Cervical horn area	35,59 P<0.001 ***	911,46 P<0.001 ***	0,00614 P<0.001 ***	57,000
Ovarian horn area vs Uterine corpus	52,66 P<0.001 ***	724,57 P<0.001 ***	0,00629 P<0.001 ***	265,500 P<0.05 *
Cervical horn area vs Uterine corpus	17.07 P<0.001 ***	186,89 P<0.001 ***	0,000143	322,500 P<0.05 *

Table 2. *Duration of Active State in norm and after oxytocin administration (M ± SEM).*

Registration areas and number of experiments, n	***Active state duration (D), min***	
	Norm	***Oxytocin administration***
Ovarian horn area (1), n = 14	0,63± 0,03	0,72±0,06
Cervical horn area (2), n = 14	0,46± 0,04	0,55±0,05
Uterine corpus (3), n = 14	0,5±0,05	0,63±0,04

Table 4. *Duration of Active State in norm, after transection, and after oxytocin administration (M ± SEM).*

Registration areas and number of experiments, n	***Active state duration (D), min***		
	Norm	***Transection***	***Oxytocin administration***
Ovarian horn area (1), n = 14	0,63± 0,02	0,45±0,01	0,63±0,05
Cervical horn area (2), n = 14	0,49±0,04	0,29±0,02	0,38±0,03
Uterine corpus (3), n = 14	0,57±0,04	0,35±0,03	0,42±0,04

The excitatory effect of oxytocin is manifested by an increase in the frequency of burst discharges and an enhancement of contractile activity [4,19]. Moreover, oxytocin may contribute to processes that ensure the integrative functioning of all rhythmogenic areas of the myometrium. In this context, analysis of the characteristics of autonomous spontaneous rhythmogenic areas of the myometrium may provide insight into the interactions between them under the influence of oxytocin.

As shown in Figure 3A, under these conditions, all three examined areas exhibited a marked increase in the action potential amplitude and rise-rate (ovarian region – by 41.85% and 36.8%, cervical region – by 39.31% and 39.77%, uterine corpus – by 40.62% and 35.84%, respectively). Thus, oxytocin promotes a nearly synchronous increase in these parameters across all investigated loci by approximately the same magnitude. An increase in the duration of active state was also observed in all registration areas (ovarian horn area – by 0.09 min, cervical horn area – by 0.09 min, uterine corpus – by 0.13 min) (Table 2).

In the next series of experiments, the effect of oxytocin on the spontaneous activity of completely isolated from each other pacemaker areas were examined. Initially, simultaneous registration of activity from all rhythmogenic loci was performed under normal conditions, after which each locus was fully isolated by transecting horns in the corresponding sites (Figure 4A). Following isolation of all regions, similar changes in activity characteristics were observed: the amplitude and spike rise- rate parameters decreased to a comparable extent in the ovarian horn area (by 31.87% and 35.56%), cervical horn area (by 31.12% and 34.21%), and uterine corpus (by 34.26% and 36.14%). For each area, the duration of the active state changed by similar values: ovarian horn area– by 0.18 min, cervical horn area – by 0.20 min, and uterine corpus – by 0.22 min (Table 3).

However, following oxytocin administration under isolation conditions, the changes in all analyzed action potential parameters differed from those observed in the other regions (Figure 4B). In the ovarian horn area, both the amplitude and rise- rate of spikes increased, approaching their values observed in norm. Notably, the duration of the active state in the isolated ovarian region also increased under oxytocin influence, reaching the level recorded before transection (Table 3).

Morphohistochemical analysis revealed the presence of distinct “physiological” states within the examined areas. In intact animals, myogenic structures in the vicinity of the ovarian horn area were more intensely stained (Figure 5A), whereas moderate staining of myogenic elements was observed in the cervical horn area and uterine corpus (Figure 5B,C). Following oxytocin administration (Figure 5D–F), an enhancement of

smooth muscle cell metabolism was observed along the entire uterine horns and uterine corpus, compared with intact animals (Figure 5A–C), with the ovarian horn area exhibiting the greatest activation (Figure 5D).

The above histochemical findings are consistent with the electrophysiological data.

Conclusion.

According to the performed analysis, oxytocin led to a marked increase in spike amplitude and rise- rate in the isolated ovarian horn area relative to other rhythmogenic areas, exhibiting the most pronounced post-transection enhancement. Under oxytocin exposure, the most pronounced enhancement of metabolic activity is also observed in the smooth muscle cells of the ovarian horn area. Hence, regions with higher Ca^{2+}-dependent acid phosphatase activity corresponded to areas of more intense electrophysiological activity, suggesting a functional link that warrants further investigation in future studies.

Based on the obtained data, it can be concluded that the ovarian area of the myometrium plays a leading role in the synchronization of activity among the different uterine areas, which display distinct electrophysiological characteristics, under the influence of oxytocin.

REFERENCES

1. Hutchings G, Williams O, Cretoiu D, et al. Myometrial interstitial cells and the coordination of myometrial contractility. J. Cell Mol. Med. 2009;13:4268-4282.
2. Domino M, Pawlinski B, Gajewska M, et al. Uterine EMG activity in the non-pregnant sow during estrous cycle. BMC Vet Res. 2018;14:176.
3. Hall J. E. Guyton and Hall Textbook of Medical Physiology 12th Edition. 2011:1120.
4. Fox S. I. Human physiology, 14th Edition. McGraw-Hill Higher Education. 2016:832.
5. Muszynski C, Happillon T, Azudin K, et al. Automated electrohysterographic detection of uterine contractions for monitoring of pregnancy: feasibility and prospects. BMC Pregnancy and Childbirth. 2018;18:13-21.
6. Buhimschi C.S, Saade G.R, Buhimschi I.A, et al. Effect of stimulatory and inhibitory drugs on uterine electrical activity measured noninvasively from the abdominal surface of pregnant rats. Am. J. Obstet. Gynecol. 2000;183:68-75.
7. Maul H, Maner W. L, Saade G.R, et al. The physiology of uterine contractions. Clin. Perinatol. 2003;30:665-676.
8. Garfield R.E, Maner W.L. Physiology and electrical activity of uterine contractions. Semin. Cell. Dev. Biol. 2007;18:289-295.
9. Dodds K.N, Staikopoulos V, Beckett E.A.H. Uterine Contractility in the Nonpregnant Mouse: Changes During the Estrous Cycle and Effects of Chloride Channel Blockade. Biology of reproduction. 2015;92:1-15.
10. Shmygol A, Blanks A.M, Bru-Mercier G, et al. Control of uterine Ca2+ by membrane voltage: toward understanding the excitation-contraction coupling in human myometrium. Ann. N. Y. Acad. Sci. 2007;1101:97-109.
11. Rabotti C, Mischi M. Propagation of electrical activity in uterine muscle during pregnancy. Acta Physiol (Oxf). 2015;213:406-416.
12. Arrowsmith S, Quenby S, Weeks A, et al. Poor spontaneous and oxytocin-stimulated contractility in human myometrium from postdates pregnancies. PLoS One. 2012;7:e36787.
13. Cavaco-Goncalves S, Marques C.C, Horta A.E, et al. Increased cervical electrical activity during oestrus in progestagen treated ewes: Possible role in sperm transport. Anim. Reprod. Sci. 2006;93:360-365.
14. Sarkisyan R.Sh, Karamyan G.G, Manukyan A.M, et al. Modern microprocessor-based equipment for electrophysiological research. International Scientific and Technical Exhibition “Digitec Expo 14”, October 1–3, Yerevan, 2014.
15. Meliksetyan I.B. Detection of Ca2+-dependent acid phosphatase activity in the cellular structures of the rat brain. Morphology, St. Petersburg. 2007;131:77-80.
16. Meliksetyan I.B, Nazaryan O.A, Sahakyan I.K, et al. Application of a histochemical method for detection of Ca2+ dependent acid phosphatase activity for studies of morpho-functional state of the cell structures in the rat brain. Neurochem. J. 2008;2:315.
17. Suvarna S.K, Layton Ch, Bancroft J.D. Bancroft's Theory and Practice of Histological Techniques Book. 2019.
18. Rabotti C, Mischi M, van Laar J.O.E.H, et al. Inter-electrode delay estimators for electrohysterographic propagation analysis. Physiol Meas. 2009;30:745-761.
19. Kasai Y, Tsutsumi O, Taketani Y, et al. Stretch-induced enhancement of contractions in uterine smooth muscle of rats. J Physiol. 1995;486:373-384.