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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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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.

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CORRELATION BETWEEN RHYTHMOGENESIS OF THE RAT URETERS UNDER HISTAMINE EXPOSURE

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Abstract.

The work is devoted to the study of the interrelationship between the characteristics of spontaneous electrical activities in paired ureters in norm and after isolation. Analysis was conducted by detecting the amplitude (A), rise rate (V), rise-time (T/2), half-width (t), and frequency of rhythmogenesis (F) of pacemaker activity. In norm, the amplitude value exceeds in the left ureter that of the right ureter. Sequential isolation of the organs (left ureter, then right) results in a decrease in the action potential amplitude by 26%, which indicates a certain interconnection between them. Additionally, histamine exposure leads to a synchronous increase in both ureters in norm. Subsequent isolation of the left ureter leads to a significant increase in the amplitude – up to 171%, and rise rate – up to 158%, of the right ureter. These findings suggest that histamine contributes to the increased excitability and regulation between the two ureters.

Thus, this hormone, by enhancing rhythmogenesis in the right ureter, may indicate certain potential for the overall functioning of the urinary system.

Key words. Ureteral rhythmogenesis, perirenal areas, transection, spontaneous activity, histamine.

Introduction.

The functional role of the urinary system is determined by the ability of the ureters to conduct an excitatory wave of activity from the renal pelvis to the urinary bladder. This process is based on the generation of electrical impulses in the form of action potentials, which contribute to the formation of contractile waves (ureteral peristalsis) [1,2].

Pacemaker potentials that are myogenic in nature, originate in the proximal region of each ureter and spread electrotonically to the resting areas of these organs, initiating action potential discharges [3-5]. It is known that ureters function in a complex with more distally located structures of the urinary system (the bladder and urethra) within a single excretory organ [6-8]. At the same time, they are characterized by identical physiological properties, with each organ possessing autonomy over its own rhythmogenesis [9,10]. Thus, this fact does not exclude the possibility of some asymmetry between the ureters.

Pacemaker activity of the ureter occurs in the renal pelvis and ensures the activity of the organ - peristalsis. While myogenic rhythm plays a primary role in ensuring the peristaltic process, neural and humoral controls are necessary to modulate and coordinate the patterns of rhythmogenesis.

Organs of the urinary system have a very specific response to the endogenous mediator, histamine. There is evidence indicating a direct effect of histamine on the smooth muscle of lymphatic vessels through the stimulation of H1 receptors [11,12]. Moreover, histamine is known to increase the contractility of the ureter [13]. It is also known that the electrical activity of the ureter is associated with the widespread presence of the above-mentioned H1 histamine receptors in the tissues of the organ, as well as the presence of mast cells that are capable of releasing histamine [14].

The presence of an intrinsic basic autonomous electrical rhythm has been identified for the paired ureters. Although each of them is characterized by their own physiological function, a certain mutual influence between the automatisms of these organs is necessary to ensure their overall integrative activity [15].

Given the close correlation between these organs, as well as the existence of various types of pacemaker activities, the question of the role of histamine in activation and resolution of the aforementioned issue is of particular interest.

Materials and Methods.

Electrophysiological study:

The study was conducted on sexually mature 11 outbred male rats weighing 250–300g. Animals were anesthetized by intraperitoneal injection of Nembutal (45–50 mg/kg) under *in situ* conditions. Surgical access to the kidney, ureter, bladder, and urethra was achieved via a midline abdominal incision. Denervation of the urinary tract organs was performed by severing the roots of the pelvic and celiac nerves, as well as the pudendal and hypogastric nerves [16].

To record electrical activity of the muscle tissue, bipolar electrodes with distance of 2 mm between the recording tips were used. Spontaneous electrical activity was recorded using a 4-channel device developed at the Orbeli Institute of Physiology of the NAS RA for assessing the electrical activity of smooth muscles. The equipment allows simultaneous recording from four areas of the studied structure. The signal-to-noise ratio

of device ensures reliable detection of signal deviations with amplitudes up to 10 μV. The bandwidth filter for the recorded signals operates in the range of 3–30 Hz.

The electrical activity was analyzed by determining the amplitude (A), rise rate (V), rise time (T) and half-width (t, the time required to form the upper part of the peak) and the spike generation frequency (F) of spontaneous action potentials.

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

Histamine (Sigma–Aldrich Chem. GmbH, Germany) optimal loading dose of 10^{-4} mol/L was administered intravenously by 0.2 ml injection volume. The substance was initially dissolved in distilled water, and the prepared solution was subsequently diluted in isotonic sodium chloride solution. The drug was administered into the femoral vein, with a single injection used in each experiment.

Histochemical study:

To investigate the morphofunctional properties of the rat ureter, a histochemical method was used to detect Ca2+-dependent acid phosphatase (AP) activity [17-20]. 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 [21]. The applied method adheres to all requirements of this principle. 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. When AP activity is tested, the phosphate ions released under the action of the enzyme can freely move in the mixture and react with different structures, regardless of their spatial arrangement, and after incubation in the solution of sodium sulfide it turns into a visible dark brown precipitate of lead sulfide. The resulting image is adequate, highly informative, and allows judgments to be made about specific links in the metabolism of the examined structures.

For histochemical analysis, the animals were anesthetized with pentobarbital (40 mg/kg, intraperitoneal) followed by ureter extraction. The extracted ureter was fixed in a 5% solution of neutral formalin prepared in 0.1 M phosphate buffer (PBS, pH=7.4) for 48 hours at +4°C. Sections of the relevant ureter regions were prepared 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. Incubation was carried out in a thermostat at 37°C for 1.5 hours. Subsequently, the sections were washed in distilled water, developed in a sodium sulfate solution, rinsed again, and mounted in balsam, followed by the light microscopy of preparations. Subsequent images of the obtained preparations were captured using the OPTON M-35 camera and the AmScope MU800 camera attachment through the OPTON microscope (West Germany).

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.

The method used in this study to record spontaneous activity allows for the examination of the electrophysiological properties of paired ureters in norm (Figure 1), as well as after isolating each one from the influence of neighboring organs.

Based on the functional similarity of the ureters, studying the interaction between them involved a comparative analysis of the characteristics of action potentials. For clarity, the evaluation of the obtained results in the percentage ratio of the right ureter to the left was carried out (Figure 2A). The amplitude and the rise - rate of peaks in the right ureter reached 75% and 77% of the corresponding parameters in the left ureter, with $P \leq 0.01$. Similar difference in percentage ratio was revealed for the frequency of rhythmogenesis. On the Figure 2D are superimposed and unfolded typical forms of action potentials for the right and left ureters. Significant difference in their parameters of activity is shown in Table 1.

Next, sequential isolation of the ureters was performed by severing them at the junction with the bladder. After acute tissue injury, stabilization of activity was established within 10–15 minutes, after which activity was evaluated. First, the left ureter was severed, followed by the right one. A decrease in amplitude by 26% and in peak rise rate by 31% was observed, while the frequency of rhythmogenesis decreased by 17%, with small changes in T/2 and t indicators (Figure 2B). As for the right ureter, with minor changes in all characteristics, only the frequency showed a reduction by 12% (Figure 2C).

Thus, despite the autonomy of each of the paired organs under study, there is a certain interconnection between their spontaneous activities.

Based on the close correlation between the paired ureters which differ in their pacemaker activities, the role of histamine in activating these processes becomes of particular interest. The influence of histamine on the spontaneous activity of each ureter

Table 1. *Parameters of spontaneous activity of the ureters 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), msec**	**Half-width of spikes (t), msec**	**Frequency of the rhythmogenesis (F), oscillations/min**
Perirenal area of the left ureter (1), n =16	56.8±5.1	196.2±19.2	280±15	270±12	27.9±2.2
Perirenal area of the right ureter (2), n =16	42.6±3.5	151.0±11.1	270±17	250±12	21.2±1.4

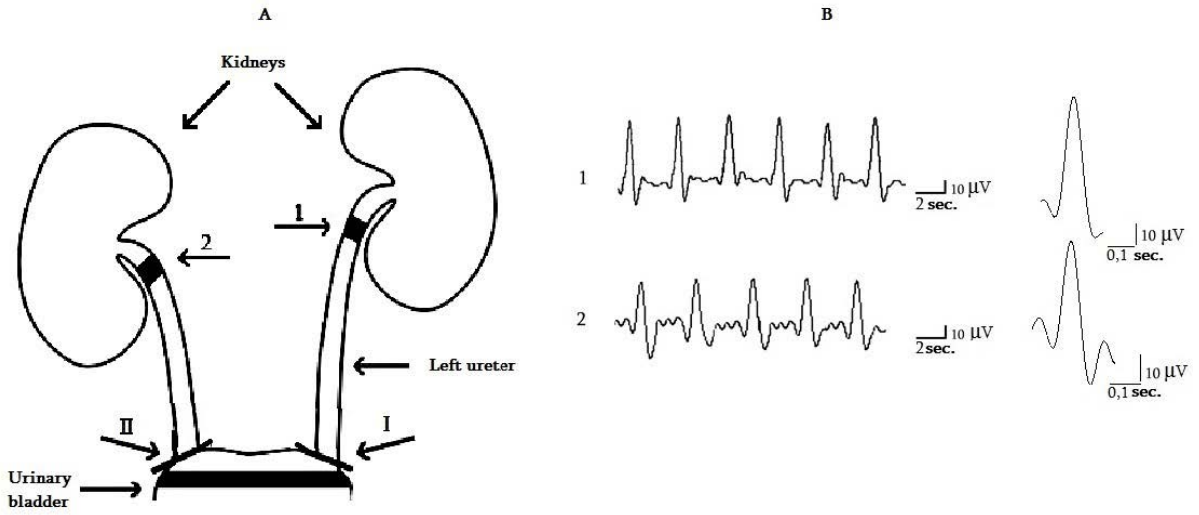

Figure 1. A. *Schematic representation of the ureters with the kidneys and bladder of in rats. 1, 2 - respective regions of activity recording from the perirenal areas of the ureters; I, II - regions where the ureters were transected.*
B. *Spontaneous action potentials recorded from the left ureter (1) and the right ureter (2). On the right, unfolded views of the action potentials from the corresponding regions are shown. n = 11.*

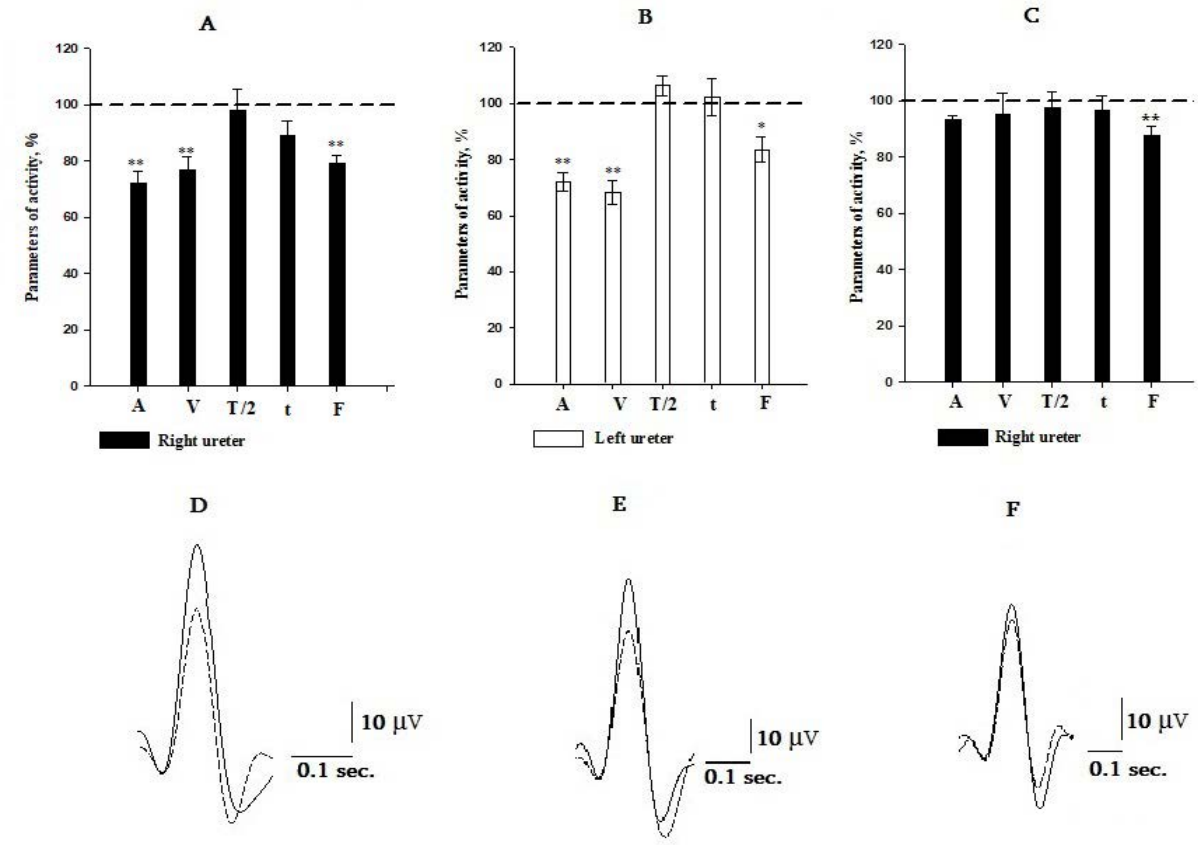

Figure 2. Comparative analysis of activity parameters of the ureters in norm and after transection.
A. Parameters of action potential of the right ureter in relation to the left, expressed in percents (the left ureteral parameters were taken as 100% - dashed line).
B. Parameters of action potential of the left ureter after transection, expressed in percents (norm was taken as 100% -dashed line).
C. Parameters of action potential of the right ureter after transection, expressed in percents (norm was taken as 100% -dashed line).
D. Superimposition of averaged action potential waveforms of the ureters. The solid line corresponds to the left ureter, and the dashed line - to the right ureter.
*E and F. Superimposition of averaged action potential waveforms of the left and right ureters in norm (solid line) and after transection (dashed line). n = 11, **P ≤ 0,01, *P ≤0,05.*

was studied by administering an optimal dose of the substance at a concentration of 10^{-4} M into the femoral vein of the animal.

Simultaneous recording of activity from the proximal regions of each ureter makes it possible to investigate changes in the nature of rhythmogenesis under the influence of histamine, both in the context of a comprehensive approach to both organs and when they are isolated from each other. Figure 3 presents the results of the analysis of the left ureter activity characteristic values before and after its transection.

The analysis was conducted as percentages relative to the norm (taken as 100%). According to Figure 3A, histamine promotes an increase in the amplitude of the action potential (by 31.2%), its rise rate (by 37.7%), and the frequency of rhythmogenesis (by 25%) in the left ureter, with minor changes in T/2 and t. However, when the ureter is isolated, a decrease in the amplitude of action potentials (by 16.2%) is observed. For the other parameters, small decreases are also noted. On the right (Figure 3B), superposition of the averaged forms of the left ureter is presented.

The analysis of the results of changes in the action potential characteristics of the right ureter under the influence of histamine was carried out under the following sequential experimental conditions: administration of histamine, transection of the left ureter, then the right ureter. The administration of histamine, similar to its effect on the left ureter, significantly and sharply increased the activity parameters of the right ureter, such as amplitude, rise rate, and frequency of rhythmogenesis (by 42%, 39.23%, and 32.5%, respectively) (Figure 4A). Transection of the more active left ureter immediately results in a further increase, primarily in the amplitude and rise rate of the right ureter, by 29.13% and 19%, respectively. Following the subsequent isolation of the right ureter, a decrease in the altered characteristic values is observed, returning to approximately the levels noted before the isolation of both ureters. The superimposed altered forms of action potentials shown in Figure 4B demonstrate changes in values and parameters. Thus, the possibility of a certain influence of the left ureter activity on the automatism of the right ureter cannot be excluded.

According to our results, histamine significantly activates both ureters. In case of higher characteristic values of the left ureter in norm, the excitatory effect of histamine is more pronounced for the amplitude of the right ureter (Figure 4A). While the isolation of the left ureter under the influence of histamine leads to a decrease in its amplitude, a simultaneous increase in this parameter is observed for the right ureter (Figures 3A and 4A).

The subsequent transection of the right ureter results in the reversal of action potential amplitude values to those observed before the transection of the left ureter (Figure 4A). It is possible that specific electrophysiological characteristics of the right ureter compensates the functional activity of the removed left ureter and contributes to the noted increase in its activity.

According to the above-mentioned, the ureters are paired organs that share the same physiological role. However, one of them may possess greater reserve capacity in regulating the integrative activity of the urinary tract organs.

Histochemical method for detecting the activity of Ca^{2+}-dependent acid phosphatase on frontal sections of intact rats has revealed cellular structures in the ureter walls. The latter consists of three layers: the inner mucosal layer, the middle muscular layer, and the outer adventitial layer. The mucosal layer is closely associated with the basal membrane and exhibits high activity of orthophosphates along the entire length of the ureter (in the perirenal, mid-ureteral, and peribladder areas) (Figures 5A and 5C).

The muscular layer lies directly adjacent to the suburothelium and consists of longitudinal and circular layers of smooth muscle fibers (Figures 5A and 5C). In the perirenal area, the smooth muscle fibers appear as discontinuous spirals with varying

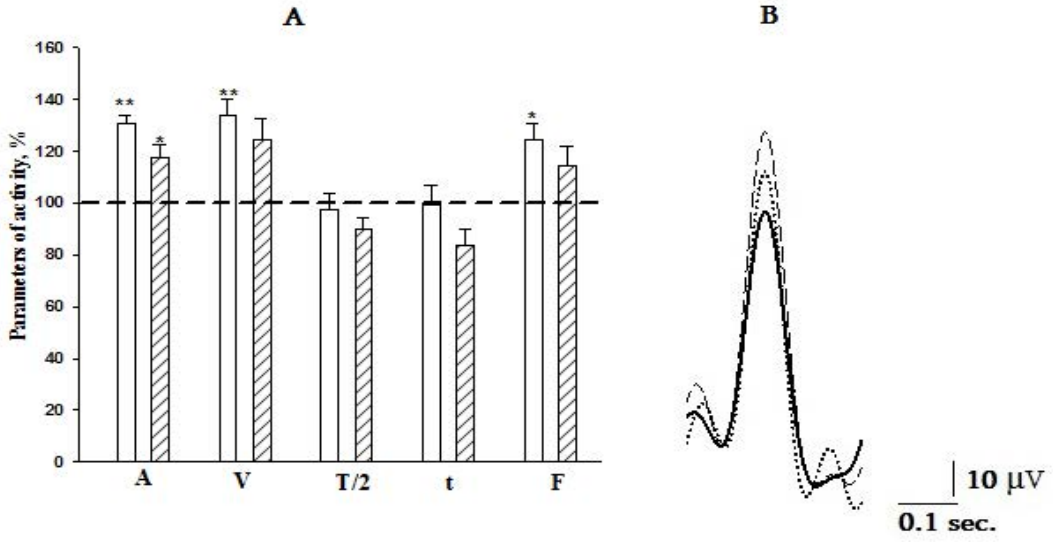

Figure 3. *Parameters of action potential of the left ureter after histamine administration (first, white bars for each parameter) and subsequent transection (second, dashed bars for each parameter) in percents (norm was taken as 100% -dashed line). B. Superimposition of averaged action potential waveforms in norm (solid outline), after histamine administration (dashed outline), and after transection (dotted outline). **P ≤ 0,01, *P ≤0,05.*

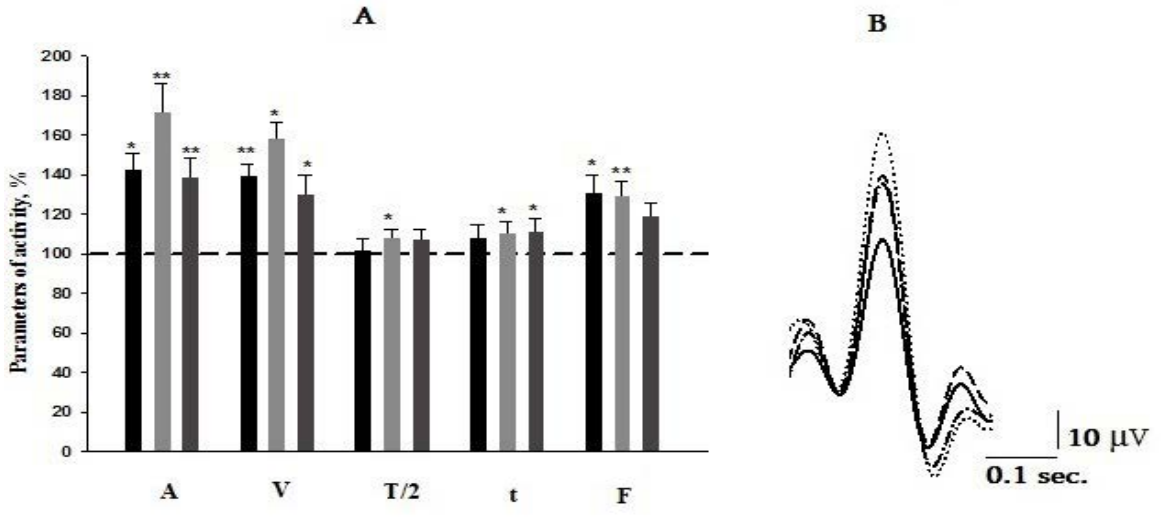

Figure 4. *Parameters of action potential of the right ureter after the introduction of histamine (first, black bars for each parameter), after subsequent transection of the left ureter (second, light grey bars for each parameter), after subsequent transection of the right ureter (third, dark grey bars for each parameter) in percents (norm was taken as 100% - dashed line). B. Superimposition of averaged action potential waveforms in norm (solid outline), after histamine administration (dashed outline), after the left ureter transection (dotted outline), and after the right ureter transection (dash-dotted outline). ** P ≤ 0.01, * P ≤ 0.05.*

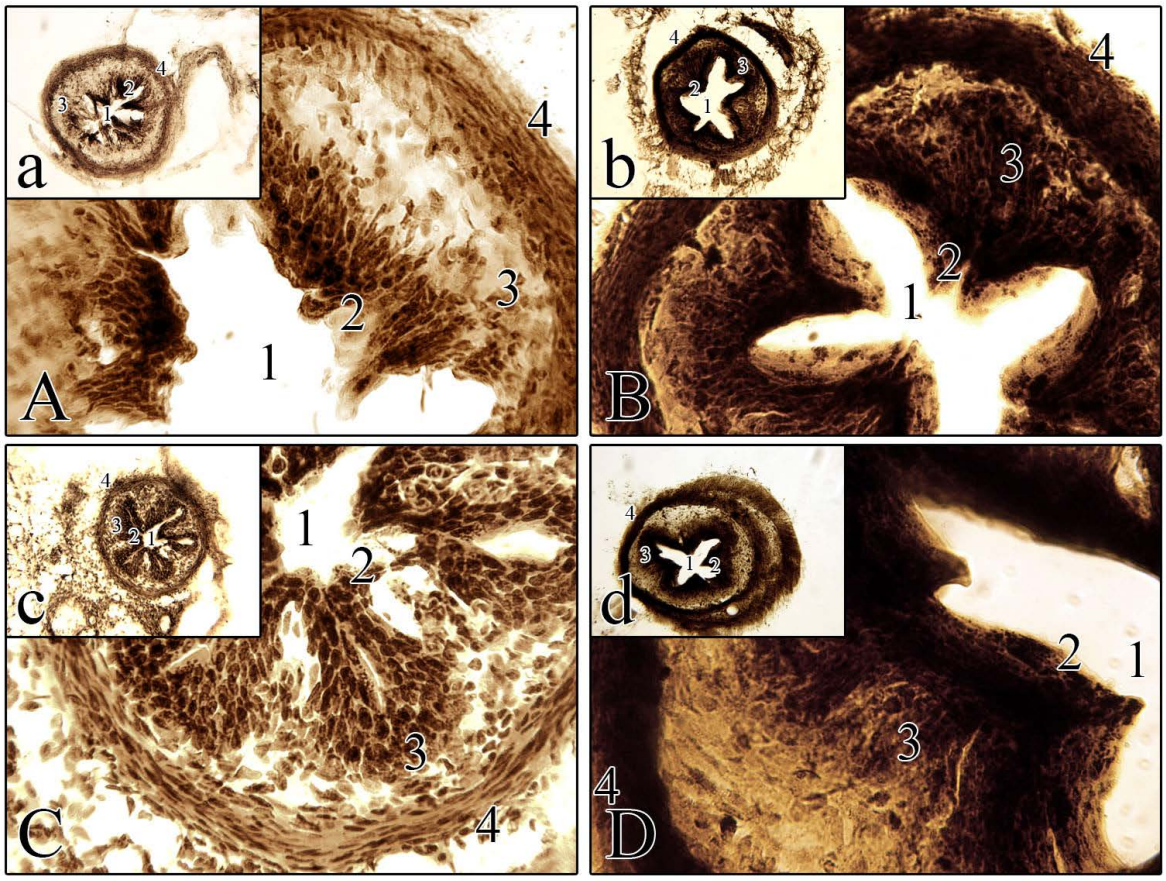

Figure 5. *Frontal sections of the perirenal (A, B) and peribladder (C, D) areas of the ureter in an intact rat (A, C) and under the influence of histamine (B, D) (1 – lumen; 2 – mucous membrane; 3 – muscle layer, smooth muscle cells; 4 – serous membrane). Method: Detection of Ca^{2+}-dependent acid phosphatase activity. Magnification: ×160 (a, b, c, d); ×400 (A, B, C, D); digital resolution: 8 MP.*

steepness (Figure 5A). In contrast to the ureteral perirenal area, myogenic structures of the wall of the ureteral peribladder area are arranged evenly, with a moderate degree of staining intensity (Figure 5C).

A morphological analysis was conducted to characterize the effects of histamine. Intense staining of the cellular elements of the muscular layer in the ureteral perirenal and peribladder areas was observed, indicating a high functional activity of those regions. Under the influence of histamine, a clear and uniform enhancement of acid phosphatase activity was observed in all the ureteral areas under consideration. The activity of acid phosphatase in the cellular structures was so enhanced that it created an impression of a diffuse darkened staining (Figure 5B and 5D). In the perirenal and peribladder areas of the ureter, under the influence of histamine, myogenic elements are clearly identified; however, compared to intact animals, intensely stained elements predominate here, accumulating in dark, granular formations throughout.

Thus, morpho-histochemical studies have shown that in both ureteral perirenal and peribladder areas histamine causes a uniform increase in acid phosphatase activity, which suggests that in response to the increased level of histamine in the body, there is a consistent increase in enzymatic activity along the entire length of the ureter.

Presented morpho-histochemical results fully support the findings of electrophysiological studies on the effect of histamine on the pacemaker activity of the ureters.

Discussion.

According to our results, histamine significantly activates both ureters. While characteristics of the left ureter were generally higher in norm, the excitatory effect of histamine was more pronounced on the amplitude of the right ureter. When the left ureter was isolated under the influence of histamine, its amplitude decreased, whereas a simultaneous increase in the same parameter was observed for the right ureter. Subsequent transection of the right ureter led to a reversal of action potential amplitude values to levels observed before the left ureter was severed (Figures 3A and 4 A). This suggests that certain electrical characteristics of the right ureter may allow it to compensate for the functional activity of the removed left ureter, contributing to the observed increase in its activity.

In the upper urinary tract, electrical impulses originate in the proximal region of the renal pelvis and have an ability to propagate distally along the organ. In contrast, in the bladder, impulse generation can occur at any point in the wall and may spread in multiple directions, with axial propagation being predominant [22].

Although ureters are paired organs, they exhibit slightly different parameters in their characteristic types of action potentials. This may be due to functional differences between the right and left ureters, with one potentially possessing greater reserve capacity in regulating the integrative activity. This difference is likely linked to the higher functional load of the left ureter in urine transport.

Thus, a possible connection between the above-described functional differences between the right and left ureters cannot be ruled out.

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