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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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THE RATIO OF EXCITATORY AND INHIBITORY SYNAPTIC PROCESSES IN NEURONS OF THE ENTORHINAL CORTEX OF THE BRAIN, ACTIVATED BY BASOLATERAL AMYGDALA ON THE MODEL OF PARKINSON'S DISEASE, UNDER CONDITIONS OF PROTECTION BY HYDROCORTISONE

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Abstract.

Parkinson disease (PD) is a common neurodegenerative condition. It affects the central nervous system, and it impairs cognitive processes, motor skills and other functions. The aim of this study was to determine the synaptic processes in medial Entorhinal cortex (mENT) under High frequency stimulation of Basolateral Amygdala on the model of Parkinson's disease under the influence of Hydrocortisone. Rotenone is involved in the degeneration of dopaminergic neurons. We investigated whether hydrocortison protects against rotenone-induced dopaminergic neurotoxicity in a rat model by in vivo electrical recording from medial Entorhinal cortex. Hydrocortison significantly improved electrical activity of neurons in the mENT of rotenone-induced PD model rats.

Key words. Parkinson's disease, synaptic processes, the entorhinal cortex, basolateral amygdala, hydrocortisone.

Introduction.

Parkinson's disease (PD) is a common disease facing many older people across the world. It affects the central nervous system, and it impairs cognitive processes, motor skills and other functions.

In addition to the classic motor signs and symptoms, PD is characterized by neuropsychological and emotional deficits, including blunting of the emotional response. Both the neural basis of abnormal emotional behavior in PD and the physiological effects of dopaminergic therapy on the response of the amygdala, the central structure of emotion processing, were investigated. The results demonstrate an abnormal amygdala response in PD, which may underlie the emotional deficit that accompanies the disease. In addition, in accordance with the conclusions of experimental animal paradigms, the results provide in vivo evidence of the role of dopamine in modulating the response of the amygdala to sensory information in humans [1]. The amygdala undergoes serious pathological changes in PD. Although evidence suggests that the basolateral amygdala (BLA) and the dorsal hippocampus work together to influence spatial/contextual learning consolidation, the circuitry mechanism by which, BLA selectively modulates spatial/context memory consolidation is not clear. The medial entorhinal cortex (mENT) is a critical area in the hippocampus-based system for processing spatial information. As an efferent target, BLA mENT is a candidate by which BLA influences the consolidation of such learning [2]. The mechanism by which the BLA affects spatial/context memory consolidation is unknown.

Rotenone is a naturally occurring toxin that inhibits complex I of the mitochondrial electron transport chain. Several epidemiological studies have shown an increased risk of Parkinson's disease (PD) in individuals exposed chronically to rotenone, and it has received great attention for its ability to reproduce many critical features of PD in animal models. Laboratory studies of rotenone have repeatedly shown that it induces in vivo substantia nigra dopaminergic cell loss, a hallmark of PD neuropathology. Additionally, rotenone induces in vivo aggregation of α-synuclein, the major component of Lewy bodies and Lewy neurites found in the brain of PD patients and another hallmark of PD neuropathology. Some in vivo rotenone models also reproduce peripheral signs of PD, such as reduced intestinal motility and peripheral α-synuclein aggregation, both of which are thought to precede classical signs of PD in humans, such as cogwheel rigidity, bradykinesia, and resting tremor. Nevertheless, variability has been noted in cohorts of animals exposed to the same rotenone exposure regimen and also between cohorts exposed to similar doses of rotenone. Low doses, administered chronically, may reproduce PD symptoms and neuropathology more faithfully than excessively high doses, but overlap between toxicity and parkinsonian motor phenotypes makes it difficult to separate if behavior is examined in isolation. Rotenone degrades when exposed to light or water, and choice of vehicle may affect outcome. Rotenone is metabolized extensively in vivo, and choice of route of exposure influences greatly the dose used. However, male rodents may be capable of greater metabolism of rotenone, which could therefore reduce their total body exposure when compared with female rodents. The pharmacokinetics of rotenone has been studied extensively, over many decades. Here, we review these pharmacokinetics and models of PD using this important piscicide [3].

The toxicity of rotenone has been demonstrated in a number of in vitro [4] and in-vivo [5-7] studies. Furthermore, it has been demonstrated that when low doses of multiple exogenous factors are combined, synergistic neurotoxicity may occur. Rotenone's effect has been attributed to the inhibition of mitochondrial complex I [8], the release of NADPH oxidase-derived superoxide from activated microglia [9] and possibly alteration of glutamate transmission [10].

As a result, novel therapies involving natural antioxidants and plant products/molecules with neuroprotective properties are being used as adjunctive therapy. Hydrocortisone is an

adrenocorticoid steroid with multiple mechanisms of action including anti-inflammatory activity, immunosuppressive properties and anti-proliferative actions.

Dysfunctional parkin due to mutations or post-translational modifications contributes to dopaminergic neurodegeneration in Parkinson's disease (PD). Overexpression of parkin provides protection against cellular stresses and prevents dopamine cell loss in several PD animal models. Scientists performed an unbiased high-throughput luciferase screening to identify chemicals that can increase parkin expression. Among promising parkin inducers, hydrocortisone possessed the most favorable profiles including parkin induction ability, cell protection ability, and physicochemical property of absorption, distribution, metabolism, and excretion (ADME) without inducing endoplasmic reticulum stress. They found that hydrocortisone-induced parkin expression was accountable for cell protection against oxidative stress. Hydrocortisone-activated parkin expression was mediated by CREB pathway since gRNA to CREB abolished hydrocortisone's ability to induce parkin. Finally, hydrocortisone treatment in mice increased brain parkin levels and prevented 6-hydroxy dopamine induced dopamine cell loss when assessed at 4 days after the toxin's injection. Our results showed that hydrocortisone could stimulate parkin expression via CREB pathway, and the induced parkin expression was accountable for its neuroprotective effect. Since glucocorticoid is a physiological hormone, maintaining optimal levels of glucocorticoid might be a potential therapeutic or preventive strategy for Parkinson's disease [11].

Most studies in PD animal models have focused on the motor features associated with dopamine depletion but still the molecular basis of PD and the molecular pathways of cell death remain unknown [12]. While cellular models have helped to identify specific events, in vivo animal models have simulated most, although not all, of the hallmarks of PD and are useful for testing new neuroprotective approaches.

The current study aims to determine the relationship of excitatory and depressor responses of single neurons during stimulation of BLA, Entorhinal cortex (ENT) of the brain, structures that control emotional memory, in order to assess the mechanisms of their defeat in a model of PD induced by unilateral administration of rotenone and the success of hydrocortisone protection in comparison with the norm.

Methods.

Experiments were performed on 9 rats of the Wistar Albino line (230±30 g). Rats were kept under typical conditions of the laboratory vivarium. The animals were provided with food and water ad libitum. The experimental protocol satisfied the provisions of European Communities Council Directive (2010/63/UE) and was approved by the Ethics Committee of Yerevan State Medical University after Mkhitar Heratsi.

Rotenone was purchased from Sigma Chemical Company (St. Louis, MO, USA).

Electrophysiological studies were performed in three experimental series: intact (n = 3), on a rotenone model of PD induced by unilateral administration of rotenone (2.5 mg/kg/day) and aged up to the experiment of 4 weeks (n = 3), under conditions of adrenalectomy (ADX) with protection by hydrocrtisone (14 injections every other day at a dose of 1mg /1ml) (n=3). The introduction of rotenone was carried out under conditions of nembutal anesthesia (40 mg / kg, w/b, 12 μg in 0.5 μl dimexide, at a rate of 1 μl/min) in the medial forebrain bundle at the coordinates of the stereotaxic atlas (AP+0.2; L±1.8; DV+8 mm) [13]. The study was conducted in accordance with the principles of the Basel Declaration and the recommendations of the ARRIVE management [14]. In the stereotaxic apparatus, trepanation of the skull from bregma to lambda was performed and the dura mater was opened. Glass microelectrodes with a tip diameter of 1-2 μM, filled with 2M NaCl, were injected into the ENT according to stereotaxic coordinates (AP-5.4; L±6.5; DV+8.3 mm) for extracellular recording of spike activity of single neurons. High-frequency stimulation (HFS) of ipsilateral BLA was carried out by means of rectangular current shocks with a duration of 0.05 ms, an amplitude of 0.12–0.18 mV, a current of 0.32 mA and a frequency of 100 Hz for 1 second, according to stereotaxic coordinates (AP-2.76; L±1.5; DV+2.9 mm) (Figure 1). Operations were performed on narcotic recorded in a stereotaxic apparatus. Activity was manifested in the form of TD and TP followed by PTP and PTD of different latency, severity and duration of animals (urethane 1.2g/kg iv). A software mathematical analysis of a single spike activity of 261 neurons was carried out. Post-stimulus manifestations of activity were evaluated by on-line registration and software mathematical analysis, which allows the selection of spike-megapixel discrimination with the derivation of "rasters" of peristimulus spiking of neurons, the construction of histograms of the sum and diagrams of the average frequency of spikes. Further, multi-level statistical processing was carried out separately for pre- and post-stimulus periods of time and the period of HFS. For the selected compared groups of neuronal activity spikes, as well as arbitrarily selected tests in a single neuron, summarized and averaged peristymulus (PETH Average) histograms and frequency histograms (Frequency Average) were constructed with the calculation of the average frequency of spikes. The analysis of the data obtained was carried out according to a specially developed algorithm that ensures the reliability of peristimulus changes in interspike intervals.

The homogeneity of the two independent samples was controlled by Student's t–criterion. In order to increase the statistical reliability of peristimulus changes in interspike intervals, the Wilcoxon-Mann-Whitney test was also used [15], as a nonparametric criterion that assesses the homogeneity of the independent two samples. Since the number of registered spikes was quite large (up to several hundred spikes in a 10-20 second interval after the stimulus), a variation of this test was used - the z-test, which determines its asymptotic normality. Taking into account critical values in comparison with those of the normal distribution at significance levels of 0.05, 0.01 and 0.001 (for various tests) shows that in most cases of spiking neuronal activity in HFS, a statistically significant change reached at least 0.05.

Results and Discussion.

Extracellular recording of spike activity of single ENT neurons was carried out in norm (56 neurons n = 3), on the

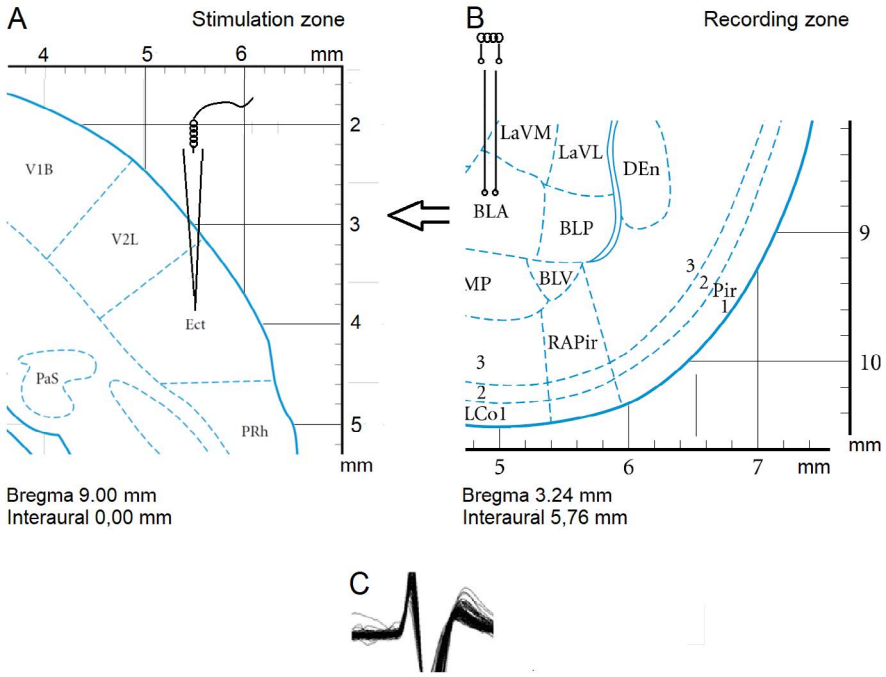

Figure 1. *Scheme of the experiment on BLA stimulation and recoding from ENT. Stereotactic image of the stimulation zone - A, the point of recording of neuronal activity - B, and the characteristic action potential - C.*

PD model under ADX (102 neurons, n = 3), with protection by hydrocortisone (103 neurons, n = 3), with exposure to 4 weeks. Through analysis based on the average number of spikes (PETH), converted to interimpulse intervals and frequencies in Hz (Frequency Average), the following changes in neuronal activity were detected.

In ENT neurons on HFS BLA, tetanic depression in both sequences in norm determined by about 2.50- and 1.50-fold decreases in prestimulus activity, respectively (Figure 2A, Groups A, B). Tetanic potentiation, accompanied by post-tetanic potentiation and depression, was detected in the range of 1.33- and 1.75-fold excess of prestimulus activity (Figure 2B, Groups A, B). In ENT neurons in HFS BLA, tetanic depression in the PD model under ADX conditions was determined within 1.43- and 1.57-fold decrease in prestimulus activity in both sequences, and tetanic potentiation was calculated on the order of 1.11 and 1.10-fold excess of prestimulus activity in the excitatory and excitatory-depressor sequence (Figures 3A, B, Group A, B). Tetanic potentiation, accompanied by post-tetanic potentiation and depression, was detected in the range of 1.33- and 1.75-fold excess of prestimulus activity (Figure 2B, Groups A, B). In ENT neurons in HFS BLA, tetanic depression in the PD model under ADX conditions was determined within 1.43- and 1.57-fold decrease in prestimulus activity in both sequences, and tetanic potentiation was calculated on the order of 1.11 and 1.10-fold excess of prestimulus activity in the excitatory and excitatory-depressor sequence (Figures 3 A, B, Group A, B). This, apparently, can't but lead to the actual suppression of both synaptic processes. Further, in ENT neurons in HFS BLA, under the conditions of hydrocortisone exposure, in both depressor sequences, tetanic depression reached a 1.66- and 2.50-fold decrease in prestimulus activity, respectively (Figure 4A, Groups A, B), and tetanic potentiation in both sequences was calculated on the order of 1.20 and 1.50 times the excess of prestimulus activity (Figure 4B, Group A, B). In other words, the protective effect of hydrocortisone is obvious, which exceeded the values of tetanic depression in both sequences. reaching 1.66- and 2.50-fold (against 1.43- 1.57-fold in pathology).

The same applies to tetanic potentiation, which reached 1.20- and 1.50-fold excess against 1.11- and 1.10 times - in pathology. However, it is necessary to postpone the conclusion until their subsequent evaluation, taking into account the pre- and post-stimulus frequency of impulse activity in these experimental conditions of distortion of post-stimulus synaptic effects, due to the excess of its frequency.

When assessing the relative severity of the above-mentioned depressor and excitatory effects, on the example of diagrams of the average frequency of spikes derived on the basis of raster of pre- and post-stimulus depressor and depressor-excitatory multidirectional manifestations of spike activity of ENT neurons in the norm, on a model of PD induced by rotenone, burdened with ADX, and under conditions of protection with hydrocortisone indicating the average digital values in real time 20 seconds before and after stimulation, including HFS time, obtained values presented in the form of disk diagrams to more clearly represent the degree of severity in the frequency display (in % and digital display) of experimental data in Figure 8 (based on Figures 5-7), which led to the following conclusion.

The values of tetanic depression in the depressor and depressor-excitatory sequence and the levels of tetanic potentiation in the excitatory and excitatory-depressor sequence of ENT neurons on HFS BLA in norm reached 1.78- and 1.34-fold reduction (Figures 5 and 8A, B), 1.46- and 1.35-fold excess (Figures 5 and 8C, D), compared with the prestimulus level of activity, respectively. As can be seen, these values differed little, which indicates the actual balance of depressor and excitatory post-

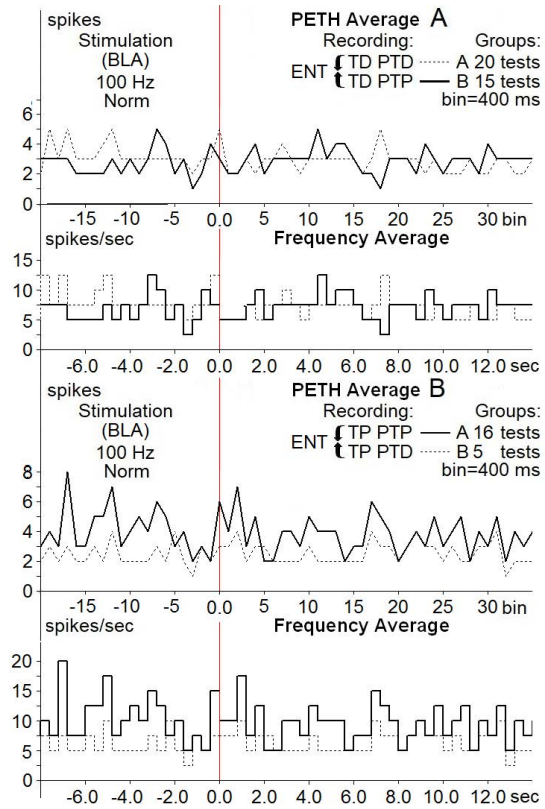

Figure 2. *Average Perievent time histograms (PETH Average) and frequency histograms (Frequency Average) of depressor, depressor excitatory (A, C, Groups A, B) and excitatory, excitatory - depressor (B, D, Groups A, B) poststimulus manifestations of ENT neurons at HFS (100 Hz, 1 sec) BLA in norm (A, B). For groups the quantity of tests has been shown (tests).*

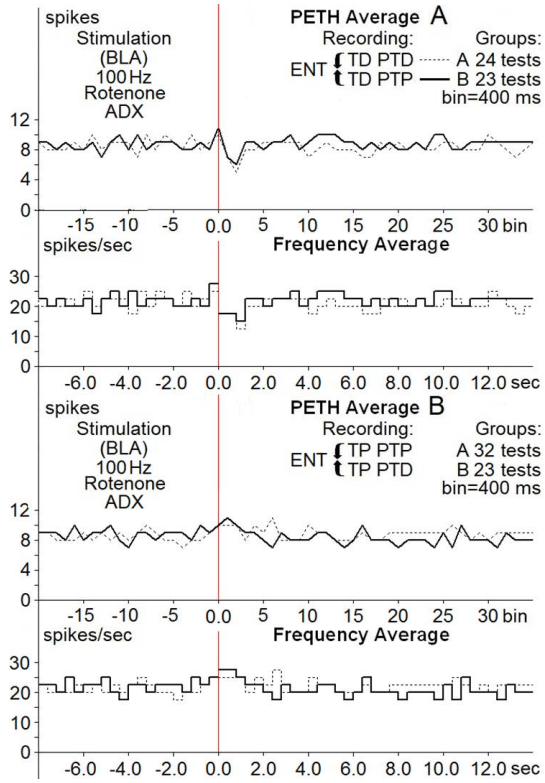

Figure 3. *Average Perievent time histograms (PETH Average) and frequency histograms (Frequency Average) of depressor, depressor excitatory (A, C, Groups A, B) and excitatory, excitatory - depressor (B, D, Groups A, B) poststimulus manifestations of ENT neurons at HFS (100 Hz, 1 sec) BLA on the model of PD in condition of ADX (A, B) For groups the quantity of tests has been shown (tests).*

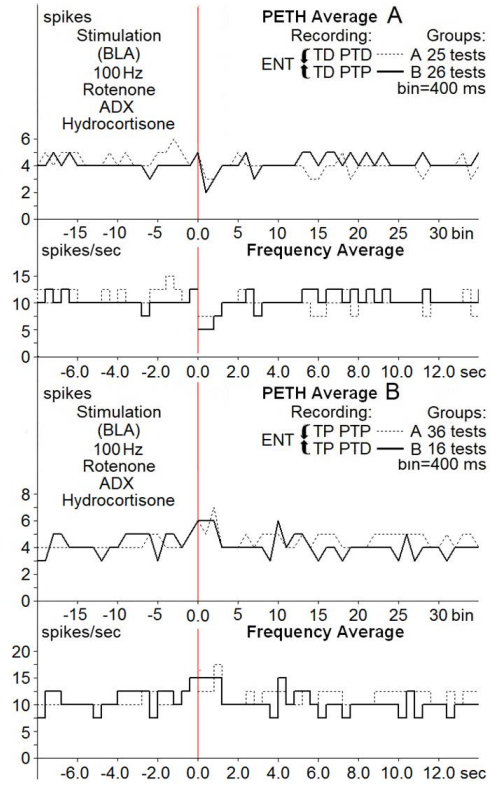

Figure 4. *Average Perievent time histograms (PETH Average) and frequency histograms (Frequency Average) of depressor, depressor excitatory (A, Groups A, B) and excitatory, excitatory – depressor (B, Groups A, B) poststimulus manifestations of ENT neurons at HFS (100 Hz, 1 sec) BLA in condition of hydrocortisone action. For groups the quantity of tests has been shown (tests).*

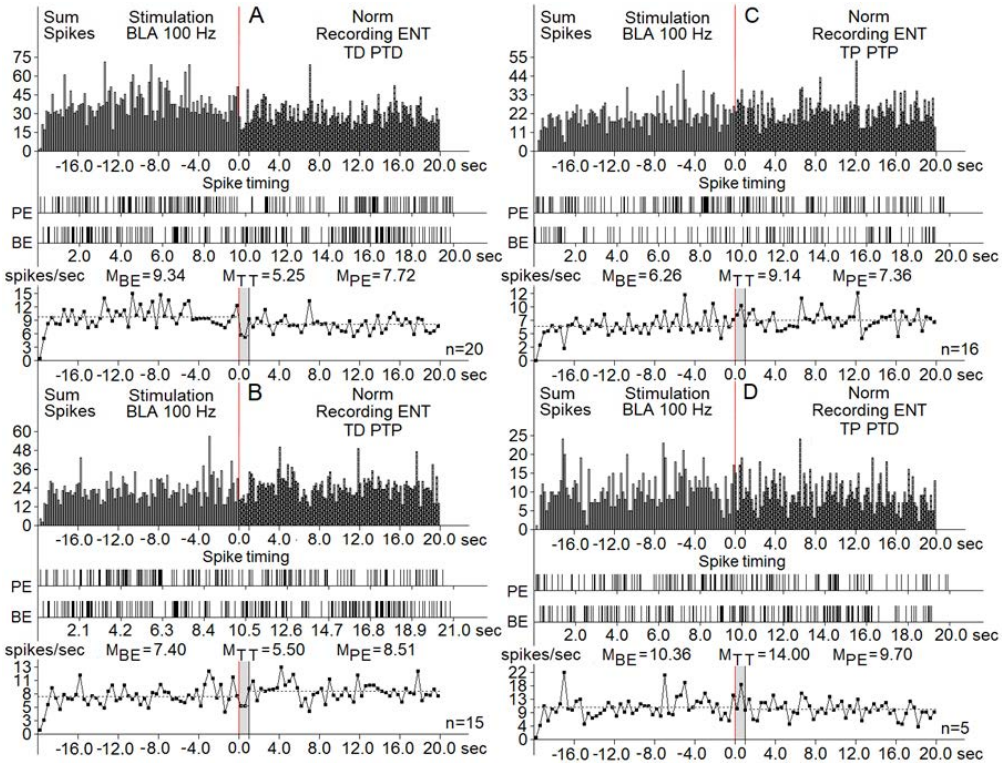

Figure 5. *A-D – histograms of sum spikes of pre- and post-stimulus tetanic depressor manifestations of activity TD PTD (A), in combination with post-tetanic excitatory – TD PTP (B), excitatory – TP PTP (C), accompanied by depressor TP PTD (D), of ENT neurons, evoked at HFS of BLA in norm in real time 20 sec (before and after stimulation). The raster of activity on A-D – the detailed analyses of arbitrarily elected single neurons from this group. Diagrams of frequency spikes, presented in histograms, with averaged values (M) for time intervals before (BE - before event), at the time being tetanization (TT - time tetanization) and after stimulation (PE - post event). To the right of the diagrams – quantity of tests (n).*

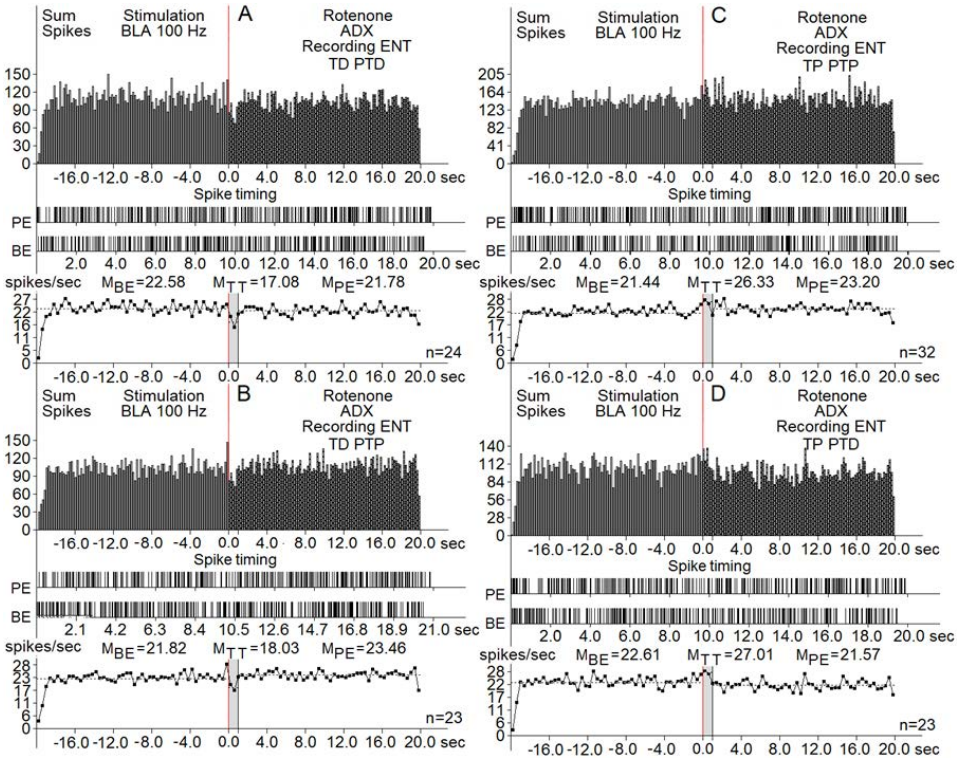

Figure 6. *A-D – histograms of sum spikes of pre- and poststimulus tetanic depressor manifestations of activity TD PTD (A), in combination with posttetanic excitatory – TD PTP (B), excitatory – TP PTP (C), accompanied by depressor TP PTD (D), of ENT neurons, evoked at HFS of BLA on the model of PD in condition of ADX in real time 20 sec (before and after stimulation). The raster of activity on A-D – the detailed analyses of arbitrarily elected single neurons from this group. To the right of the diagrams – quantity of tests (n).*

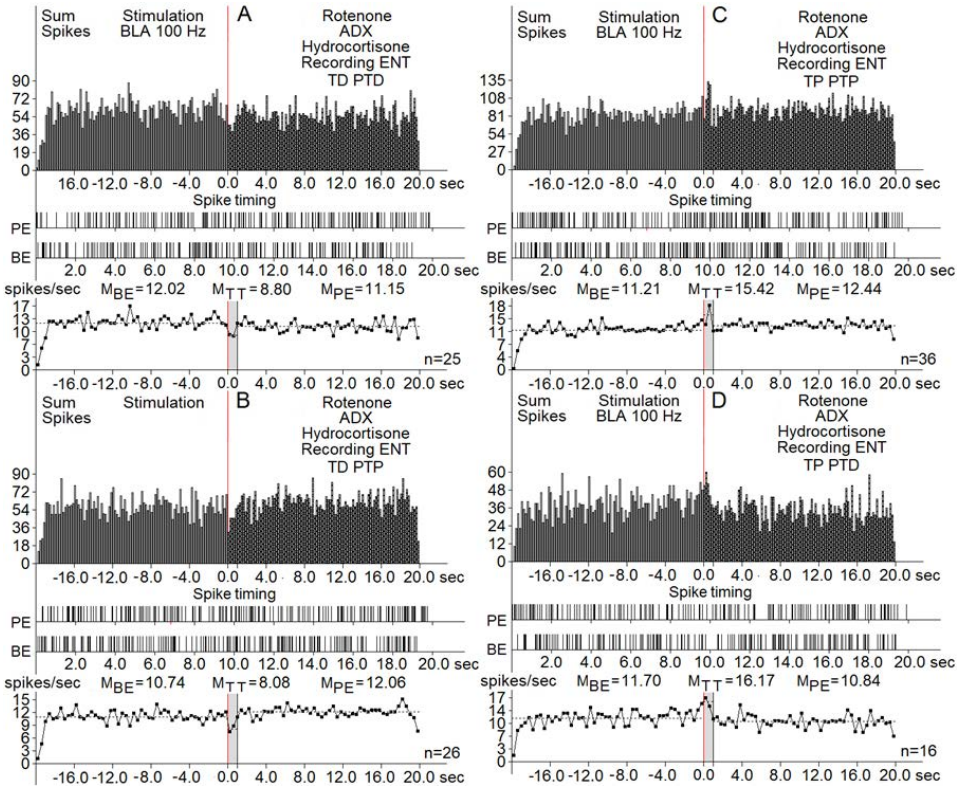

Figure 7. *A-D – histograms of sum spikes of pre- and poststimulus tetanic depressor manifestations of activity TD PTD (A), in combination with posttetanic excitatory – TD PTP (B), excitatory – TP PTP (C), accompanied by depressor (D), of ENT neurons, evoked at HFS of BLA on the model of PD in condition of ADX with protection by hydrocortisone in real time 20 sec (before and after stimulation). The raster of activity on A-D – the detailed analyses of arbitrarily elected single neurons from this group. To the right of the diagrams – quantity of tests (n).*

stimulus manifestations of the activity of the studied neurons in the norm. The values of tetanic depression in the depressor and excitatory succession of ENT neurons on HFS BLA, in comparison with the prestimulus level of activity on the PD model under ADX conditions, differed significantly with this type of analysis, in comparison with the norm (1.32- and 1.21 versus 1.78- and 1.34-fold, respectively) (Figures 5,6 and 8 A-D), which will be discussed later with a different type of evaluation of the results.

In the ENT neurons on HFS BLA, the values of tetanic depression and the levels of tetanic potentiation in both post-stimulus sequences on the PD model with ADX under the conditions of hydrocortisone protection were calculated in the range of 1.36- and 1.33-fold reduction and 1.38 and 1.37-fold excess of prestymulus activity (Figures 5-7 and 8A-D). In other words, taking into account only the multiplicity of measurements of comparative indicators of these post-stimulus effects in pathology, in comparison with those in the conditions of protection, there were unexpressed shifts.

An interesting, in addition, more pronounced picture was found when comparing the frequency of pre- and post-stimulus activity of ENT neurons on HFS BLA under these experimental conditions. The predominant frequency of activity preceding the depressor effects in the norm and on the PD model with ADX reached multiples of 9.34, 7.40 and 22.58, 21.82, respectively (Figures 5,6 and 8E, F) and preceded by excitatory sequences in norm and pathology - 6.26, 10.36 and 21.44, 22.61, respectively (Figures 5, 6 and 8 E, F).

It is obvious that there is a significant excitotoxicity in the PD model, in comparison with the norm indicating pronounced neurodegeneration preceding both depressor and excitatory post-stimulus effects (3.42- and 2.20-fold prevailing, respectively), which was to be expected.

The prestimulus frequency of activity in ENT neurons preceding depressor and excitatory sequences, under conditions of hydrocortisone protection, was calculated in the range of 12.02, 10.74, 11.21 and 11.70, respectively, compared with 9.34. 7.40, 6.26. 10.36 in norm and 22.58, 21.82, 21.44, 22.61 in pathology without protection (Figures 5-7 and 8 E-H).

In other words, in pathology with protection, the prestimulus frequency of activity preceded by depressor post-stimulant effects decreased by 1.87-, 2.03-fold, and the one preceded by excitatory effects - 2.01-, 2.03-fold, with a real approximation to the norm. Thus, under the conditions of protection, in comparison with pathology, there was an obvious and significant decline in the prestimulus frequency preceded by depressor and excitatory post-stimulus effects, and therefore excessively overestimated toxic excitability, which clearly indicates in favor of protection by hydrocortisone, which is more than successfully coped with excitotoxicity.

As for the post-stimulus frequency of activity of ENT neurons, then normally, being accompanied by depressor and excitatory post-stimulant effects, it reached 5.25, 5.50, 9.14 and 14.001, and on the PD model with ADX - 17.08, 18.0, 27.01 and 27.01 (Figures 5, 6 and 8 I-L). In other words, on the PD model with ADX, the post-stimulus frequency, accompanied by depressor reactions, significantly exceeded the norm of 3.25- and 3.28-fold, and accompanied by excitatory - 2.88- and 2.03-fold, in pathology without protection. Thus, in general, there was a powerful increase in the frequency of post-stimulus activity, indicating again, as in the case of the prestimulus frequency, a huge excitotoxicity (Figures 5,6 and 8 I-L). Further, under protection conditions, there was a sharp decrease in the frequency of post-stimulus activity on the PD model, accompanied by depressor and excitatory activity (within 2.04-, 2.05 and 1.71-, 1.67-fold, respectively) with an actual approximation to the norm of such, accompanied by depressor (8.80 and 8.08 vs. 5.25 and 5.50) and excitatory (15.42 and 16.17 vs. 9.14 and 14.00) (Figures 5-7 and 8 I-L). In conclusion, the PD model in condition of ADX revealed a powerful excitotoxicity, which the used protection with hydrocortisone successfully copes.

Excitotoxicity in neurodegenerative diseases, which occurs as a compensatory response to a decrease in excitation as a result of neuronal death, damages them by overactivation of glutamate NMDA and AMPA receptors [16], thereby causing neuronal apoptosis and subsequent death [17,18]. Excitotoxicity is accompanied by impaired calcium buffering, free radical generation, activation of mitochondrial permeability, and secondary excitotoxicity [19]. The noted, according to the concept put forward in a recently published report, indicates the need for deepening, in conditions of neurodegeneration, depressor effects that carry a protective load and reduce excessive excitatory reactions [20,21].

Conclusion.

In three series of experiments on 9 Albino rats (230±30g), an analysis of the impulse activity of 261 single neurons of the Entorhinal cortex (Entorhinal cortex - ENT) of the brain with high-frequency stimulation (HFS): baso-lateral amygdala (Basolateral amygdala - BLA) in norm (n = 3), on a rotenone model of Parkinson's disease (PD), induced by unilateral administration of rotenone and aged up to the experiment 4 weeks (n = 3) and under ADX conditions with protection with hydrocortisone (n = 3). Based on the softvare mathematical analysis of the degree of severity of the average frequency of post-stimulus depressor and excitatory synaptic effects of ENT neurons, in comparison with the prestimulus level of activity, it was revealed. In the norm, a 1.78- and 1.34-fold decrease in depressor post-stimulus tetanic and post-tetanic synaptic effects and a 1.46- and 1.35-fold excess of such excitatory effects. I.e. actual balance.

On the PD model with ADX, in comparison with the norm, the indicated levels of postsynaptic activity in this type of analysis reached 1.32-, 1.21-fold reduction and 1.23-. 1.20- a multiple excess of prestimulus activity, which at this level of analysis does not allow to objectively judge an important indicator of neurodegeneration - excitotoxicity, which will be discussed later. Under the conditions of hydrocortisone exposure, the values of tetanic depression and the levels of tetanic potentiation in both poststimulus sequences were calculated within 1.36-, 1.33-fold reduction and 1.37-, 1.38-fold excess of prestimulus activity, with a certain tendency to approach the norm. In other words, taking into account only the multiplicity of measurements of comparative indicators of these post-stimulus effects in pathology, in comparison with those in the conditions

of protection, there were insignificant shifts. Analysis of the pre- and post-stimulus frequency of activity of ENT neurons on HFS BLA, preceded and accompanied by depressor and excitatory post-stimulus effects in pathology and with protection, revealed more pronounced changes. The predominant frequency of activity preceding depressory and excitatory post-stimulus effects in the PD model with ADX was 22.58-, 21.82-fold reductions and 21.44 and 22.61 times higher, which, in comparison with the norm, indicates a significant excitotoxicity on the PD model with ADX. The prestimulus frequency of activity in ENT neurons preceding the depressor and excitatory sequences under conditions of hydrocortisone protection decreased to 12.02, 10.74- and 11.21, 11.70, respectively, with a real approximation to the norm, which clearly indicates in favor of protection, more than successfully coping with excitotoxicity. The post-stimulus frequency of ENT neurons in the PD model with ADX, accompanied by depressor and excitatory effects, also significantly exceeded the norm: 17.08, 18.03 and 26.33, 27.01, respectively, i.e. 17.08-, 3.28- and 2.88-, 2.02-fold, respectively, which also indicates enormous excitotoxicity. Under the conditions of hydrocortisone protection on the PD model with ADX, there was a sharp decrease in the post-stimulus frequency of activity of ENT neurons on HFS BLA, accompanied by depressor and excitatory activity (within 2.04-, 2.05- and 1.71-, 1.67-fold) with an actual approximation to the norm of such, accompanied by depressor (8.80, 8.08 vs. 5.25 5.50) and excitatory (15.42, 16.17 vs. 9.14, 14.00).

Our study provides evidence for the therapy of Parkinson's disease as well as the underlying mechanism of Hydrocortison's neuroprotective activity. Given the intricacy of molecular and neurological systems, more research is needed to pinpoint the precise process.

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Соотношение возбуждающих и тормозных синаптических процессов в нейронах энторинальной коры головного мозга, активируемых базолатеральной амигдалой на модели болезни паркинсона, в условиях защиты гидрокортизоном

Овсепян В.С, Араджян Г.М*, Абдулвааб Аль-Чачани, Мушегян Г.Х, Саркисян Дж, Габриелян И. Г. Аннотация

Болезнь Паркинсона (БП) — распространенное нейродегенеративное заболевание. Она поражает центральную нервную систему и нарушает когнитивные процессы, двигательные навыки и другие функции. Целью данного исследования было определение синаптических процессов в медиальной энторинальной коре (mENT) при высокочастотной стимуляции базолатеральной миндалины на модели болезни Паркинсона под влиянием гидрокортизона. Ротенон участвует в дегенерации дофаминергических нейронов. Мы исследовали, защищает ли гидрокортизон от вызванной ротеноном дофаминергической нейротоксичности в модели крысы с помощью in vivo электрической регистрации из медиальной энторинальной коры. Гидрокортизон значительно улучшил электрическую активность нейронов в mENT у крыс с моделью БП, вызванной ротеноном.

Ключевые слова: болезнь Паркинсона, синаптические процессы, энторинальная кора, базолатеральная миндалина, гидрокортизон.

ამგზნები და ინჰიბიტორული სინაფსური პროცესების თანაფარდობა ენტორინალური ქერქის ნეირონებში, რომლებიც გააქტიურებულია ბაზოლატერალური ამიგდალით პარკინსონის დაავადების მოდელში, ჰიდროკორტიზონით დაცვის პირობებში.

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პარკინსონის დაავადება (PD) არის გავრცელებული ნეიროდეგენერაციული დაავადება. ის გავლენას ახდენს ცენტრალურ ნერვულ სისტემაზე და აზიანებს კოგნიტურ პროცესებს, მოტორულ უნარებსა და სხვა ფუნქციებს. ამ კვლევის მიზანი იყო სინაფსური პროცესების დადგენა მედიალურ ენტორინალურ ქერქში (mENT) ბაზოლატერალური ამიგდალის მაღალი სიხშირის სტიმულაციის დროს პარკინსონის დაავადების მოდელში ჰიდროკორტიზონის გავლენის ქვეშ. როტენონი მონაწილეობს დოფამინერგული ნეირონების დეგენერაციაში. ჩვენ გამოვიკვლიეთ, იცავს თუ არა ჰიდროკორტიზონი როტენონით გამოწვეული დოფამინერგული ნეიროტოქსიურობისგან ვირთხების მოდელში, რომელიც იყენებს in vivo ელექტრო ჩანაწერებს მედიალური ენტორინალური ქერქიდან. ჰიდროკორტიზონმა მნიშვნელოვნად გააუმჯობესა ნეირონების ელექტრული აქტივობა მენტენტში ვირთხებში როტენონით გამოწვეული PD მოდელით.

საკვანძო სიტყვები: პარკინსონის დაავადება, სინაფსური პროცესები, ენტორინალური ქერქი, ბაზოლატერალური ამიგდალა, ჰიდროკორტიზონი