GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 6 (339) Июнь 2023

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.

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Содержание:

GEORGIAN MEDICAL NEWS
No 6 (339) 2023

EFFECTS OF DIMETHYL SULFOXIDE ON HIPPOCAMPAL ACTIVITY IN A ROTENONE-INDUCED RAT MODEL OF PARKINSON'S DISEASE

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Abstract.

Parkinson's disease (PD) is the second most common age-related neurodegenerative disease worldwide. The goal of this study was to examine the effects of dimethyl sulfoxide (DMSO) in a rat model of Parkinson's disease caused by rotenone. Due to its capacity to increase the penetration of potential water-insoluble drugs into the central nervous system, DMSO has been widely used in preclinical and clinical studies. Background and evoked spike activities were recorded in the hippocampus of rats administered DMSO (1 ml/kg i.p. for 3 weeks). We showed that pyramidal cells and Nissl bodies in the hippocampal CA1 and CA3 areas of rats administered rotenone dramatically improved after DMSO treatment. Rotenone enhanced TP and induced a milder TD effect, while DMSO also enhanced TP but induced a stronger TD effect.

The analysis revealed inhibitory effects in the hippocampus in response to high-frequency stimulation (HFS; 100 Hz for 1 s) of the ipsilateral entorhinal cortex.

Key words. Parkinson disease, DMSO, hippocampus, rotenone.

Introduction.

Parkinson's disease (PD) is the second most common age-related neurodegenerative disease worldwide. The animal model of Parkinson's disease known as the rotenone rat model is well-known and has undergone significant research [1]. Detailed neuropathological results in this paradigm show that rotenone promotes motor impairment without significantly destroying dopaminergic neurons [2,3]. As structural and functional abnormalities of this region have been seen in individuals with sporadic [5,6] and hereditary variants of the illness, the hippocampus is implicated in the memory difficulties seen in Parkinson's disease [4,5]. Additionally, behavioral alterations and memory problems are linked to hippocampal abnormalities [7,8]. Drugs that are insoluble in water are routinely dissolved in dimethyl sulfoxide (DMSO). As a solvent for different pharmacological drugs, it is often utilized in both in vitro and in vivo neurology investigations [9]. The biological effects of DMSO, notably in neurology, have been the subject of several investigations. Na+, K+, and Ca2+ currents, for instance, are inhibited by DMSO [10]. In Aplysia ganglion cells, acetylcholine, glutamate, and GABA all enhance membrane permeability, which is inhibited by DMSO [11]. Additionally, DMSO reduces the activation of NMDA receptors on hippocampal neurons and inhibits NMDA and AMPA currents [9]. DMSO crosses the blood-brain barrier and is effective in treating traumatic cerebral edema by lowering intracranial pressure and increasing cerebral blood flow without changing blood pressure [12].

This study's main objectives were to measure the activity of hippocampal neurons in a rotenone model of Parkinson's disease and determine how DMSO affected male rats following rotenone treatment.

Materials and methods.

Animals

Ten 200–240 g-weight male Wistar rats served as the subjects for this investigation. Rats were housed in polycarbonate cages with five rats per cage in a thermostatically controlled environment with 12 hours of light and 12 hours of darkness, a temperature of 24 °C, and 45% relative humidity. During the whole trial, the rats' body weights were tracked.

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

Experimental design

Ten rats were randomly allocated into 2 groups. Rotenone was administered subcutaneously to Group A (rotenone) every other day for 21 days at a dosage of 2.5 mg/kg diluted in sunflower oil (Sigma-Aldrich). 1% DMSO (Sigma-Aldrich, St. Louis, MO, USA; 1 ml/kg; i.p.) was administered to Group B (DMSO-treated) for 21 days (rotenone 3 weeks + DMSO 3 weeks).

In vivo extracellular recording (Single-unit Recording)

All rats were terminated humanely after the 6-week research period using deep urethane anesthesia (1.1 g/kg, i.p.). Dithylinum was used to immobilize the animals at 1% (25 mg/kg, i.p.). Rats that had been anesthetized and shaved were put in a stereotactic frame and given artificial breathing. The rat brain atlas stereotaxic coordinates (AP – 3.2-3.5; L ± 1.5-3.5; DV +2.8–4.0 mm) were used to repeatedly insert a microelectrode filled with a 3 M KCl solution into the hippocampus in order to record extracellular spike activity from hippocampal neurons. [13]. Bipolar silver electrodes were used to provide rectangular current impulses with a length of 0.05 ms and an amplitude of 0.6–0.8 mA to the ipsilateral entorhinal cortex (EC) during high-frequency stimulation (HFS, 100 Hz for 1 sec) (Figure 1). The stereotaxic coordinates AP -9, L 3.5, and DV +4.0 mm were used to place a stimulating electrode into the ipsilateral entorhinal cortex. According to our earlier investigations, the Student's t-test and Mann-Whitney U test were used to examine the statistical significance of the heterogeneity of interspike intervals (or spike frequencies) of the pre- and post-stimulus impulse flow [14-16].

Morphological study (Nissl staining):

The rats were euthanized 6 weeks after receiving rotenone and DMSO treatments, and their brains were then preserved in a 4% formalin solution in phosphate buffer at pH 7.4 following each electrophysiological experiment. Serially frozen slices of the hippocampus underwent two phosphate buffer washes

before being dyed for 30 minutes with a 0.5% cresyl violet acid solution. The samples were then graded into ethanol solutions (70%, 95%, and 100%) and rinsed in distilled water. The slices were then cleaned in xylene twice, for five minutes each. After that, the slices were covered with organic mounting media made of dibutyl phthalate, polystyrene, and xylene [14]. A digital camera and a light microscope were used to capture histology pictures at the hippocampus level after drying. Using a rat brain atlas, histological preparations were examined [15].

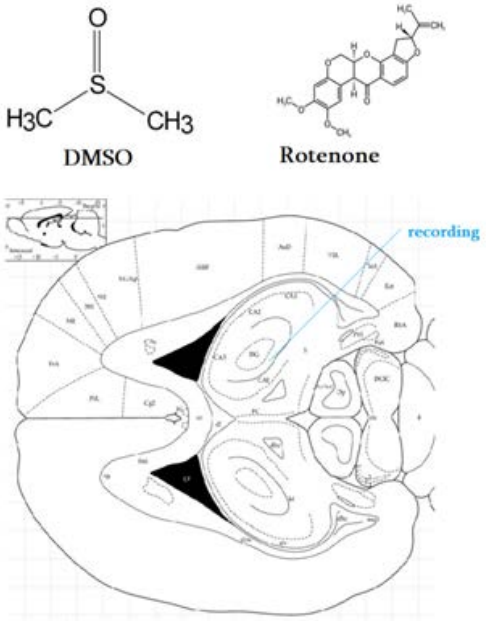

Figure 1. *Structures of Rotenone and DMSO. Rat brain (hippocampus) in the stereotaxic coordinates of Paxinos and Watson. The blue line indicates electrode placement.*

Results and Discussion.

Assessment of expression of excitatory and inhibitory responses of hippocampal neurons in response to ipsilateral entorhinal cortex HFS

The essential characteristics of these cells have been discussed in detail earlier [16], and extracellular recordings of hippocampal neurons were utilized to explore the effects of rotenone and DMSO. Tetanic potentiation in the hippocampus with TP was 2.65 times (MTT= 39.69 / MBE = 14.96 spike/sec) during HFS (100 Hz for 1 s) in the rotenone group (Figure 2, A), and TP PTP responses were 1.96 times (MTT= 23.39 / MBE = 11.93 spike/sec). The TP responses are significantly different between the rotenone and DMSO groups ($p < 0.05$). Tetanic depression occurred during HFS at a rate of 4 times in neurons with TD PTD responses (MBE = 35.69 / MTT = 8.91 spike/s) and at a rate of 5 times in neurons with TD responses (MBE = 42.18 / TT = 8.42 spike/sec) in the DMSO group (Figure 2, B).

Histological study:

We found that rotenone caused profound morphological changes in the hippocampal cells. Although neurons in the hippocampus retained staining intensity after rotenone toxicity, they were wrinkled. The hippocampal cells exhibited irregular staining. The structure of the Nissl substance was disrupted. Some neurons showed signs of edema. There was a redistribution of tigroids to the periphery of some neurons. Pyknosis of most neurons was observed in the rotenone group (Figure 3). Pyknotic neurons are characterized by small size, well-defined oblong forms, and intense chromatophilic substances (or Nissl bodies) in the cytoplasm. Their nuclei had a diffuse basophilic appearance, an elongated or triangular form, and their nucleoli were almost invisible.

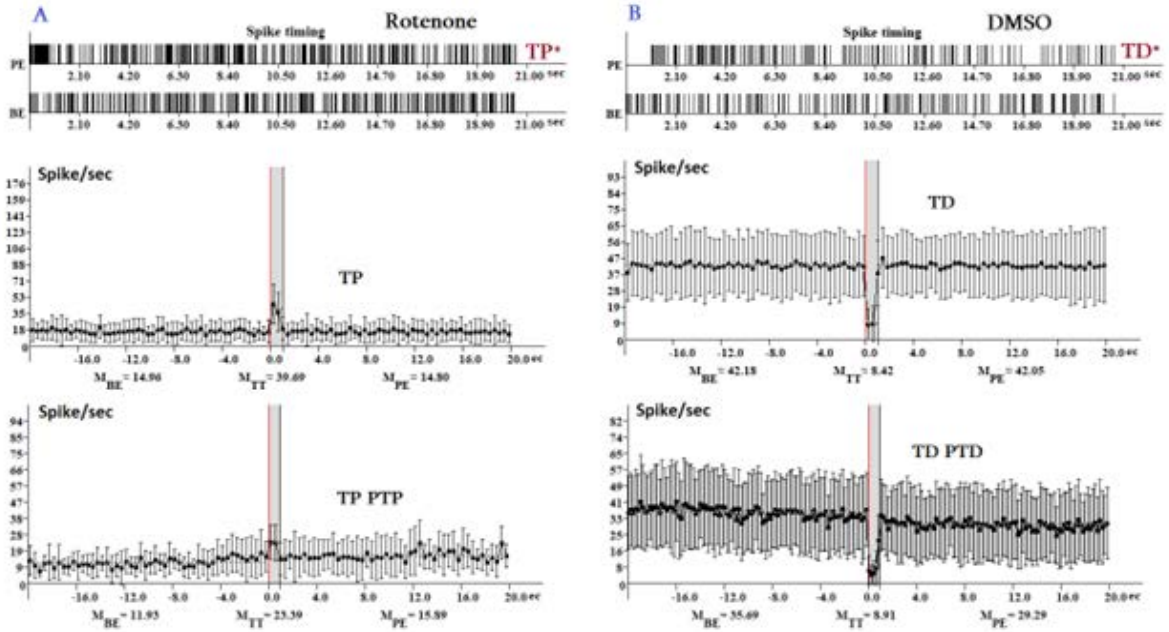

Figure 2. *Effects of rotenone and DMSO on hippocampal neuronal activity. Examples of spike activity in a single neuron include real-time impulse flow 20 s before (BE, before the event) and 20 s after stimulation (PE, post-event) (TP* and TD* effects). Hippocampal neurons showing TP, TP PTP, TD, and TD PTD responses in real-time for 20 s before HFS (M BE), 20 s after HFS (M PE), and during HFS (M HFS), were measured for their mean spike frequency.*

As shown in Figure 4, DMSO group neurons were characterized by round to oval nuclei. The chromatophilic substances of these neurons were evenly distributed in the cytoplasm as lumps with light spaces. The presence of both hyperchromic and hypochromic-stained cells characterizes the morphology of the hippocampus in the DMSO group. The processes are traced at a short distance, cell contours are visible, and light nuclei can be observed in some neurons. In general, the state of nervous tissue is characterized by varying degrees of functional activity due to the presence of hyperchromic neurons (Figure 4).

In this study, we examined how three weeks of rotenone and DMSO treatment affected hippocampal neuronal activity and neuronal response properties in rats. The toxic effects of rotenone and DMSO-treatment on hippocampal CA1 and CA3 cells were compared. We found that the DMSO group had fully developed neurons in the hippocampus, replete with nucleoli that were easily visible, faintly colored cytoplasm, and orderly organization. The rotenone group, on the other hand, had notable cell shrinkage, amorphous cell morphology, cell membrane shrinkage, pyknotic and darkly pigmented nuclei, loosely distributed hippocampal cells, fewer pyramidal cells, and fewer Nissl bodies. Pyramidal cells and Nissl bodies in the hippocampus CA1 and CA3 areas of rats given rotenone therapy dramatically improved after DMSO treatment (Figures 3 and 4).

Based on these findings, it can be inferred that rotenone, an inhibitor of mitochondrial complex I, affects synaptic plasticity in the hippocampus differently compared to the DMSO group. The rotenone group showed increased tetanic potentiation, indicating enhanced synaptic strength and plasticity in response to high-frequency stimulation. This suggests that rotenone may modulate the excitability of hippocampal neurons. The strength of the inhibitory responses to HFS in the DMSO group was higher than in the rotenone group (Figure 2). Excitatory reactions to HFS were more mildly expressed in the DMSO group than they were in the rotenone group. TD and TD PTD were expressed significantly in hippocampal neurons (65% and 30%, respectively). We concluded that an increase in inhibitory signaling following DMSO treatment counteracted the system hyperexcitability caused by the toxic effects of rotenone. An imbalance between excitement and inhibition brought on by synaptic alterations enables the body to adjust to new pathogenic situations. Because of the dynamic nature of the excitation/inhibition balance, the circuit can work in a switch-like manner to amplify brief bursts of high-frequency activity and send signals with place-field-like characteristics. [17]. The two inputs have opposing plasticity: excitation promotes spike integration, whereas feed-forward inhibition inhibits it [18]. Previously, using the same animal paradigm of rotenone-induced Parkinson's disease, we found that hippocampal neurons exhibited a preponderance of excitatory activity during HFS of the entorhinal cortex [19].

Due to its miscibility with water and capacity to promote membrane permeability, DMSO is an organic solvent that is employed as a vehicle for the absorption of substances that are insoluble in water on their own. DMSO's effects change based on the cells, experiment type, and concentration. In cell cultures, DMSO has been shown to directly impact cell excitability by changing Ca+2, K+, Na+, and Cl- currents [20,21]. NMDA and AMPA currents were repressed, and NMDA receptor activation was reduced in cultured neurons by DMSO [9]. On the other hand, rat dorsal ganglionic neurons' GABA-induced currents are inhibited by DMSO [21]. Ex vivo and in vivo investigations revealed a region-specific increase in spine density in the hippocampus of APPSDL mice treated with DMSO. DMSO also has a noticeable impact on mice's behavior, enhancing hippocampal-dependent spatial memory accuracy, regulating hippocampal-independent olfactory habituation, and having anxiolytic effects [22]. DMSO has been shown to have behavioral effects in adult rats, including effects that may reflect changes in cortical and/or hippocampal activity [23,24].

A preferred neuroprotective agent is DMSO. In cases of severe brain damage, DMSO is an efficient neuroprotective drug against secondary cell death [25]. Ex vivo and in vivo, DMSO administration led to a region-specific increase in spine density in the hippocampus of APPSDL mice. Drugs that prevent aberrant Na+ influx into the brain cells exhibit considerable neuroprotective action in animal models of brain ischemia/hypoxia. Additionally, a number of clinical trials are presently being conducted to examine how this class of medications would affect cerebral ischemia [26,27]. Since DMSO blocks Na+ channels, it explains why it has neuroprotective properties in brain cells after physical injury and ischemic stroke [28]. LTP in the CA1 region is altered by the pharmacological modulation of D1/D5 receptors [29]. This modulation correlates with memory tasks [30], implying that the loss of dopamine innervation of the hippocampus leads to impaired LTP, contributing to memory deficits in Parkinson's disease. Furthermore, rotenone has been shown to inhibit the delayed rectifier K+ current [31] while increasing the ATP-sensitive K+ current [32] and Ca2+-activated high-conductance K+ channels [33]. It has been shown to increase NMDA-induced currents in dopaminergic substantia nigra neurons [34,35]. CA1 neurons in the striatum and hippocampal nucleus are extremely vulnerable to ischemia and metabolic stress [35,36].

Surprisingly, inhibiting inhibitory GABAergic transmission is harmful, especially when there is a lack of energy, and positive GABA modulation may be a possible neuroprotective tactic in clinical circumstances with high energy demands [36]. When GABA (A) and GABA (B) receptors are co-activated, ischemia in vitro is protected against neurodegeneration. The hippocampus is less vulnerable to rotenone's complex I inhibition than the striatum, according to earlier studies [37], but mounting data supports our conclusion that the hippocampus is considerably toxic to rotenone [19]. A key component of the brain responsible for many learning and memory processes is the hippocampus. Since the hippocampus is widely known to be extremely susceptible to oxidative stress, mitochondrial products like ATP and ROS play a crucial role in hippocampal synaptic transmission [38]. In mHippoE-18 (mouse hippocampal neurons), rotenone causes cell death [39]. Hippocampal LTP was disrupted, and hippocampal-dependent memory was altered in a transgenic mouse model of α-synuclein aggregation created by expressing human α-syn120 under the control of the tyrosine hydroxylase promoter [40,41]. Overall, these results indicate that rotenone and DMSO can modulate synaptic plasticity in the hippocampus, but they have opposite effects on TP and TD

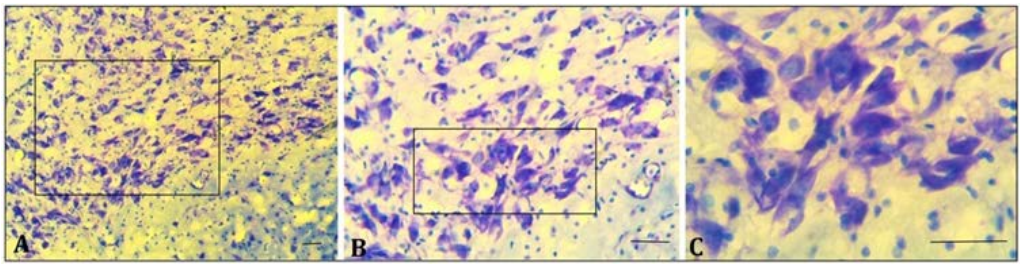

Figure 3. *Nissl staining of hippocampal neurons in the rotenone group. Scale: A-C 100 µm.*

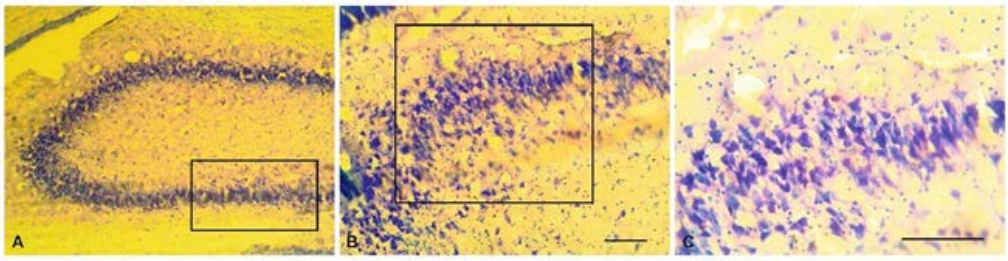

Figure 4. *Nissl staining of hippocampal neurons in DMSO-treated rats. Scale: A-C 100 µm.*

responses [42-44]. Rotenone enhances TP and induces a milder TD effect, while DMSO also enhances TP but induces a stronger TD effect. These findings suggest that rotenone and DMSO may have differential impacts on the excitability and plasticity of hippocampal neurons.

In conclusion, the rat rotenone model mirrored the pattern of functional impairments seen in Parkinson's disease in hippocampal neurons, and DMSO changed neuronal excitability.

Acknowledgments.

We would like to thank Dr Susanna Hakobyan for histological studies.

L. V. Darbinyan, K.V. Simonyan, L.E. Hambardzumyan, L.P. Manukyan confirm the absence of any conflicts over commercial or financial relations, relations with organizations or individuals that could in any way be related to the study, and in interrelations between the co-authors.

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РЕЗЮМЕ

Болезнь Паркинсона является вторым по распространенности нейродегенеративным заболеванием во всем мире. Целью данного исследования было изучение эффектов диметилсульфоксида (ДМСО) на модели болезни Паркинсона, вызванной ротеноном. Из-за его способности увеличивать проникновение потенциально нерастворимых в воде лекарственных препаратов в центральную нервную систему, ДМСО широко используется в клинических и предклинических исследованиях. Фоновая и вызванная спайковая активность регистрировалась в гиппокампе крыс, которым вводили ДМСО (1 мл/кг, внутрибрюшинно в течение 3 недель). Мы показали, что пирамидальные клетки и тела Нисля в гиппокампальных областях CA1 и CA3 крыс, получавших ротенон, значительно улучшились после лечения DMSO. Ротенон усиливал ТП и вызывал более слабый эффект ТД, тогда как DMSO также усиливал ТП, но вызывал более сильный эффект ТД.

Анализ выявил тормозные эффекты в гиппокампе в ответ на высокочастотную стимуляцию (ВЧС; 100 Гц в течение 1 с) ипсилатеральной энторинальной коры.