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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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PROTECTIVE EFFECTS OF *CURCUMA LONGA* IN A ROTENONE-INDUCED RAT MODEL OF PARKINSON'S DISEASE: ELECTROPHYSIOLOGICAL AND BEHAVIORAL EVIDENCE

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Abstract.

Parkinson's disease (PD) is characterized by progressive dopaminergic neurodegeneration leading to motor deficits, yet effective neuroprotective therapies remain limited. *Curcuma longa* (turmeric), a traditionally cultivated spice in Southeast Asia, exhibits potent antioxidant properties that may counteract neurodegenerative processes. This study investigated the neuroprotective potential of orally administered turmeric extract (1100 mg/kg) in a rotenone-induced rat model of PD. Rats received rotenone (2.5 mg/kg) for 21 days to induce PD-like pathology, followed by concurrent turmeric treatment. Neuroprotective outcomes were assessed using in vivo electrophysiology and the Cylinder test to evaluate motor function and forelimb use asymmetry. Turmeric extract administration significantly prevented rotenone-induced degenerative changes and motor impairments, indicating preservation of neuronal integrity and function. These findings suggest that turmeric extract mitigates rotenone-induced neurotoxicity, supporting its potential as a therapeutic agent for PD. Further studies are warranted to elucidate the underlying molecular mechanisms and optimize dosing strategies.

Key words. Parkinson's disease, *curcuma longa*, hippocampus, rotenone, cylinder test.

Introduction.

Parkinson's disease (PD) is a progressive neurodegenerative condition that predominantly impacts movement. It arises due to the gradual degeneration of dopamine-producing neurons located in the substantia nigra, a region in the brain. This neuronal loss results in hallmark motor symptoms such as tremors, muscle stiffness, slowness of movement (bradykinesia), and difficulties with balance and posture. In addition to these motor issues, PD is associated with various non-motor symptoms, including cognitive impairments, mood-related disorders, sleep disturbances, and dysfunctions in autonomic processes. While the precise cause of Parkinson's disease remains unclear, researchers believe it involves a complex interplay of genetic predispositions and environmental influences [1-3]. Treatment for PD aims to manage symptoms and improve quality of life, typically involving medications that increase dopamine levels in the brain, such as levodopa, dopamine agonists, MAO-B inhibitors, and COMT inhibitors [4].

Turmeric (*Curcuma longa*), a perennial plant from the ginger family (Zingiberaceae), is widely cultivated in regions such as India, China, Indonesia, Sri Lanka, Brazil, Peru, Africa, and Australia (Figure 1). Its rhizomes contain 1-5% curcuminoids, with curcumin being the primary bioactive compound responsible for its therapeutic properties. The plant lacks a stem and features rootstocks, with lance-shaped or oblong leaves that can grow up to 1 meter long. Its flowers are sterile, pale yellow with reddish coverings, and the flowering bracts exhibit green and purplish tones. The rhizomes are known for their aromatic smell and bitter taste [5,6]. The chemical composition of turmeric, particularly curcuminoids like curcumin, underpins its health benefits. Historically used in traditional medicine systems like Ayurveda and Chinese medicine, turmeric has been valued for treating a variety of ailments such as skin diseases, respiratory disorders, gastrointestinal issues, and wounds. Modern research highlights its potential in addressing conditions like inflammation, joint pain, asthma, eczema, allergies, and mood regulation. Additionally, it supports blood sugar balance and immune system modulation [7,8]. This versatile plant continues to be studied for its wide-ranging applications in food, pharmaceuticals, and biotechnology due to its safety profile and bioactive effects [5,6,8].

C. longa contains carbohydrates, fiber, certain proteins, and lipids (excluding cholesterol), along with essential nutrients such as vitamin C, pyridoxine, magnesium, phosphorus, potassium, and calcium, making it a nutritionally rich natural food ingredient. A total of 719 constituents have been identified across 32 Curcuma species, including terpenoids, flavonoids, phenylpropene derivatives, alkaloids, diphenylalkanoids, steroids, and other compounds. The rhizome of *C. longa* contains over 235 phytoconstituents, primarily polyphenols and terpenoids. Curcuminoids are the most abundant polyphenols and consist of approximately 80% curcumin [9,10]. The plant composition includes moisture (>9%), curcumin (5–6.6%), extraneous matter (<0.5%), mold (<3%), and volatile oils (<3.5%). Monoterpenes dominate the essential oils in its flowers and leaves, while sesquiterpenes are predominant in oils from roots and rhizomes. Key oil components include tumerone (25%), curdine (11.5%), and ar-turmerone (8.55%). Recent analysis has revealed that the rhizome's essential oil content is approximately 3.97%, with ar-turmerone (40%), α-turmerone (10%), and curlone (23%) as major constituents identified through gas chromatography [11,12]. Traditionally, dried curcumin powder has been used in medicine for its antitoxic, anticancer, antibacterial, anti-inflammatory, and antioxidant properties. Curcumin is a lipophilic flavonoid that is practically insoluble in water but remains stable under the stomach's acidic conditions. Its antioxidant activity is comparable to vitamins C and E in both aqueous and fat-soluble forms. Furthermore, curcumin exhibits neuroprotective effects by targeting inflammation and oxidative stress—critical factors in the progression of neurodegenerative diseases such as Parkinson's disease (PD). Studies suggest curcumin's potential

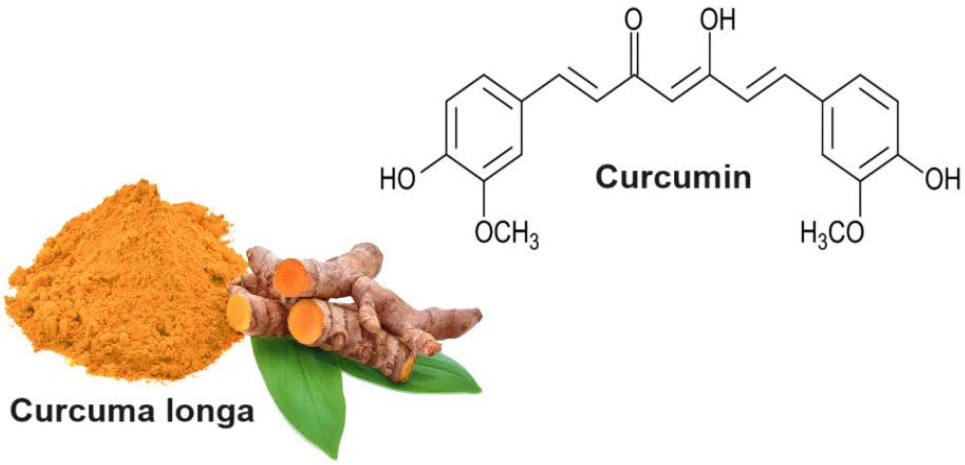

Figure 1. *Curcuma longa (Turmeric).*

as an effective therapeutic agent for mitigating PD progression [13-15].

The ethanol extract of *Curcuma longa (C. longa)* has been shown to exhibit neuroprotective effects, particularly against neuronal loss induced by dexamethasone treatment in the hippocampus of rats. Research demonstrated that pretreatment with *C. longa* extract significantly restored neuronal densities in the CA1 and dentate gyrus regions, though it did not prevent astrocyte loss, suggesting partial protection through non-oxidative mechanisms. Additionally, studies on rats exposed to trimethyltin revealed that *C. longa* extract improved spatial memory and preserved pyramidal neurons in the CA2–CA3 regions, highlighting its antioxidant and anti-inflammatory properties [16]. Further investigations have explored the extract's ability to mitigate oxidative stress and enhance enzymatic antioxidant defenses in the brain. Exploring these effects in various animal models, including aquatic species, could provide valuable insights into neuroprotective mechanisms [17,18]. The ethanolic turmeric extract has been shown to have neuroprotective effects against trimethyltin-induced neurotoxicity in rats. The extract prevented oxidative stress by decreasing plasma and brain malondialdehyde levels, and increasing reduced glutathione levels and the activities of superoxide dismutase, catalase, and glutathione peroxidase enzymes in the brain. These effects were comparable to those of citicoline, a drug used for the treatment of neurodegenerative disorders [17]. The neuroprotective effects of *C. longa* extract have been attributed to its antioxidant properties, which help reduce lipid peroxidation and increase the activities of antioxidant enzymes. The extract has been found to reduce lipid peroxidation by 35% in the rat hippocampus and increase the activity of glutathione peroxidase by 50% [17].

This study aimed to investigate the protective effects of *Curcuma longa* extract in a rotenone-induced rat model of Parkinson's disease, using electrophysiological and behavioral assessments to evaluate its potential in mitigating neurodegeneration and motor deficits.

Materials and Methods.

Animals: This study was carried out on 15 male Wistar rats weighing 200–240 g. Rats were kept in polycarbonate cages with five rats per cage, in a room maintained at a controlled temperature of 24°C and a relative humidity of 45%. They were kept on a 12-hour light/12-hour dark cycle and provided ad libitum access to food and water. Throughout the experiment, the body weights of the rats were regularly monitored. The experimental procedures followed the guidelines outlined in the European Communities Council Directive (2010/63/UE) and were approved by the Ethics Committee of the Yerevan State Medical University after Mkhitar Heratsi (Approval code: N4 IRB APPROVAL, November 15, 2018).

Experimental design:

15 rats were randomly allocated into 3 groups. 1. Control group (received sunflower oil 1 ml/kg). 2. Group rotenone every other day for 21 days at a dosage of 2.5 mg/kg diluted in sunflower oil (Sigma-Aldrich). Rotenone was administered subcutaneously to Group rotenone. 3. Rotenone+Curcuma group: Curcuma (1100 mg/kg body weight) was administered to rotenone-treated rats for 21 days (rotenone 3 weeks + Curcuma 3 weeks).

Statistical analyses:

For electrophysiological data analysis we used t-criteria of Student's t -test, the reliability of differences of interspike intervals before, after and during HFS. All p-values were determined by a two-sample unpaired Student's t-test. The spread of the data where indicated is the SD of the mean. To increase reliability of statistical evaluations, we also used the non-parametric method of verification by application of Wilcoxon two sample test. Significant differences between the obtained values were analyzed using GraphPad Prism software (version 5.0) using one-way ANOVA, followed by Tukey's post hoc test.

***In vivo* extracellular recording:**

The study involved humane termination of all rats after a 6-week experimental period using deep urethane anesthesia (1.1 g/kg, i.p.), followed by immobilization with dithylinum (25 mg/kg, i.p.). Anesthetized and shaved rats were placed in a stereotactic frame and provided artificial ventilation. Using rat brain atlas stereotaxic coordinates (AP – 3.2–3.5; L ± 1.5–3.5; DV +2.8–4.0 mm), a microelectrode filled with 3 M KCl

solution was repeatedly inserted into the hippocampus to record extracellular spike activity from hippocampal neurons [19]. Bipolar silver electrodes delivered rectangular current impulses (0.05 ms duration, 0.6–0.8 mA amplitude) to the entorhinal cortex (AP -9, L± 3.5, DV +4.0 mm) during high-frequency stimulation (HFS, 100 Hz for 1 sec). Statistical analyses of interspike intervals and spike frequencies before and after stimulation were performed using the Student's t-test and Mann-Whitney U test. This methodology allowed precise electrode placement and reliable recording of neural activity, supporting further exploration of hippocampal functions and responses to stimulation in rodent models.

Cylinder test:

The cylinder test is a widely used behavioral assessment to evaluate sensory-motor function, particularly in experimental models of PD [20]. This simple test measures spontaneous forelimb use asymmetry, a hallmark of motor deficits caused by unilateral degeneration of the nigrostriatal pathway. In the test, rodents are placed in a transparent glass cylinder, and their interactions with the cylinder walls are observed. The number of wall touches made by the left, right, or both forelimbs is recorded, often using slow-motion video analysis. Results are expressed as the percentage of usage for each paw relative to the total number of touches [21].

Results and Discussion.

***In vivo* electrophysiology:**

In the control group, in response to high-frequency stimulation of the entorhinal cortex, the comparative analysis of hippocampal impulse activity after 3 weeks in the PD model revealed stimulatory and inhibitory effects of TP and TD, followed by PTP activity. In the group of animals that received rotenone, the following impulse activities in hippocampal neurons were observed (Figure 3): excitatory responses during high-frequency stimulation and the post-stimulation period accounted for 10.2%, inhibitory responses during high-frequency stimulation and the post-stimulation period accounted for 25.51%, mixed-type responses during high-frequency stimulation and the post-stimulation period were at 30.95%, and non-reactive responses (Figure 3) were at 8.16%. Additionally, the average stimulatory stimulus responses were expressed 2.88 times during the HFS (Figure 3), while inhibitory responses were at 4.26 times (Figure 3), and mixed-type responses (TD PTP Figure 3) were at 4.1 times. In comparison, in the control group, these responses were respectively expressed 4.02 times (TD Figure 2) for stimulatory responses, 4.78 times (TD PTP Figure 2) for inhibitory responses.

In the turmeric (Curcuma) group, the TP PTD responses were significantly increased by 3 times compared to the rotenone group. Specifically, 26% TD, 19% TD PTP, 4% TP PTD, 48.5% TP PTP, and 3% TP responses were recorded in the group of rats that received *Curcuma longa* (Figure 4).

Behavioral analysis: Cylinder test.

A two-way ANOVA was conducted to analyse the effects of treatment group and forelimb on the number of rears. The results revealed significant effects for both treatment group ($F(2, 6) = 10.67$, $p < 0.05$) and forelimb ($F(1, 6) = 12.00$, $p < 0.05$). Additionally, there was a significant interaction effect between treatment group and forelimb ($F(2, 6) = 6.00$, $p < 0.05$). Tukey's HSD post hoc tests were performed to compare differences between groups and forelimbs. For treatment groups, the Control group differed significantly from both the Rotenone group ($p < 0.05$) and the Curcuma group ($p < 0.05$), while there was no significant difference between the Rotenone and Curcuma groups ($p > 0.05$) (Figure 5).

For forelimbs, there was no significant difference between the left and right forelimbs in the Control group ($p > 0.05$), but significant differences were observed between the left and right forelimbs in both the Rotenone ($p < 0.05$) and Curcuma ($p < 0.05$) groups. The Control group showed a higher number of rears compared to the Rotenone and Curcuma groups ($p < 0.05$).

The significant interaction effect suggests that the impact of treatment group on the number of rears varies depending on the forelimb, indicating differential effects of treatment on motor behavior. The statistical analysis highlights significant differences in motor behavior between treatment groups and forelimbs (Figure 5).

Ongoing research explores new treatment approaches for PD, including neuroprotective therapies to slow disease progression [22]. Advances in deep brain stimulation (DBS) and other surgical interventions offer options for advanced stages of the disease. [23]. While PD is progressive with no cure, research advancements provide hope for better management and quality of life for individuals with PD. *Curcuma longa*, commonly known as turmeric, exhibits multiple mechanisms of action within the brain that contribute to its therapeutic benefits. Turmeric increases brain levels of serotonin and norepinephrine while reducing acetylcholinesterase activity [24]. Turmeric helps reduce oxidative DNA damage and lipid peroxidation [25]. Turmeric enhances brain-derived neurotrophic factor (BDNF) production and activates cAMP response element binding protein (CREB) [26]. Turmeric regulates GABAergic transmission [24]. Turmeric modulates sodium ion channel activity [26]. Turmeric reverses decreased levels of monoamines (serotonin, noradrenaline, and dopamine) in the brain. These mechanisms support the use of *Curcuma longa* and its primary constituent curcumin in managing epileptic seizures, improving spatial memory, and protecting against age-related cognitive decline and neurodegenerative disorders like Alzheimer's and Parkinson's disease [26]. Clinical trials have investigated the effects of curcumin on memory and mood in older adults. A twice-daily dose of curcumin was found to improve both memory and mood. Curcumin’s ability to cross the blood-brain barrier suggests its potential impact on brain function [28].

In electrophysiological studies, the comparison between the rotenone group and the control group highlights significant differences in the patterns and frequencies of these impulse activities. Specifically, the rotenone group exhibited lower rates of stimulatory responses, higher rates of inhibitory and mixed-type responses, and a notable proportion of non-reactive responses compared to the control group. The average stimulatory stimulus responses, inhibitory responses, and mixed-type responses were also quantitatively different between the rotenone group and the

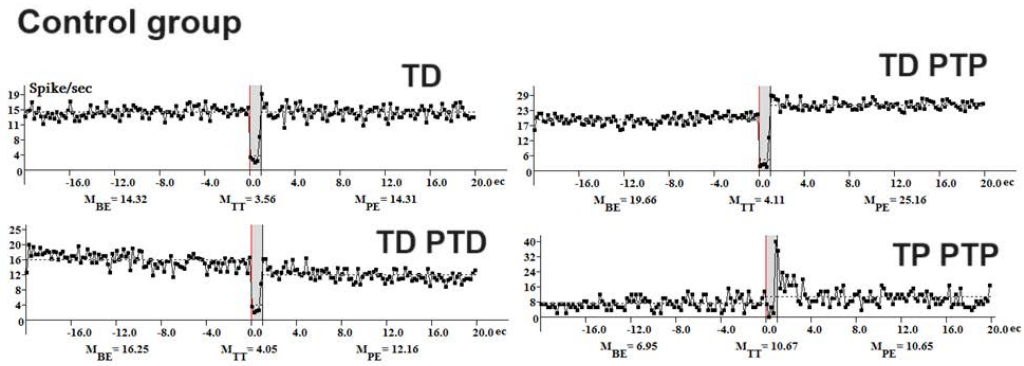

Figure 2. *Hippocampal neuronal activity in the control group. Examples of spike activity in a single neuron include real-time impulse flow 20 sec before (BE, before the event) and 20 sec after stimulation (PE, post-event).*

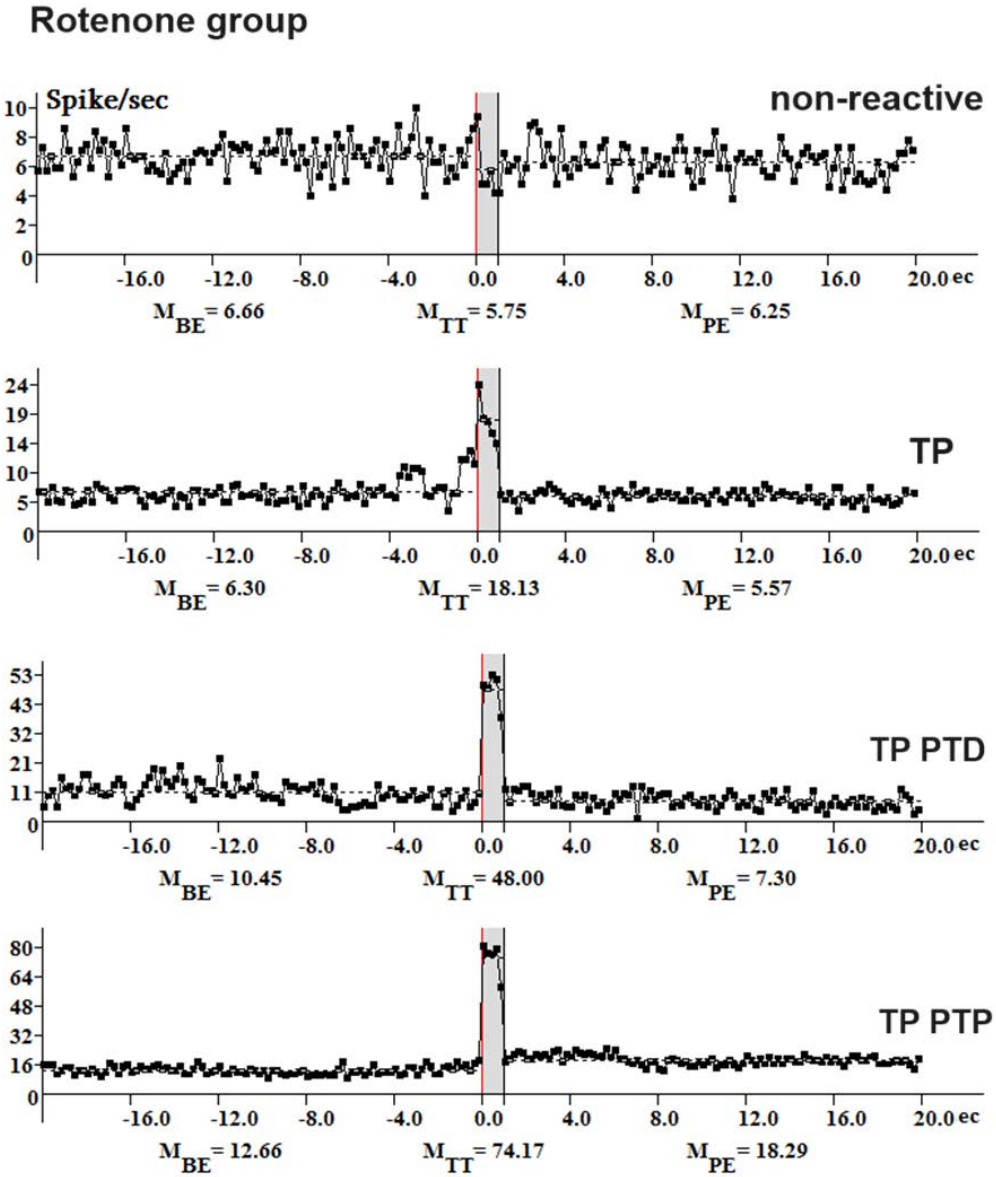

Figure 3. *Effects of Rotenone on hippocampal neuronal activity. Examples of spike activity in a single neuron include real-time impulse flow 20 sec before (BE, before the event) and 20 sec after stimulation (PE, post-event).*

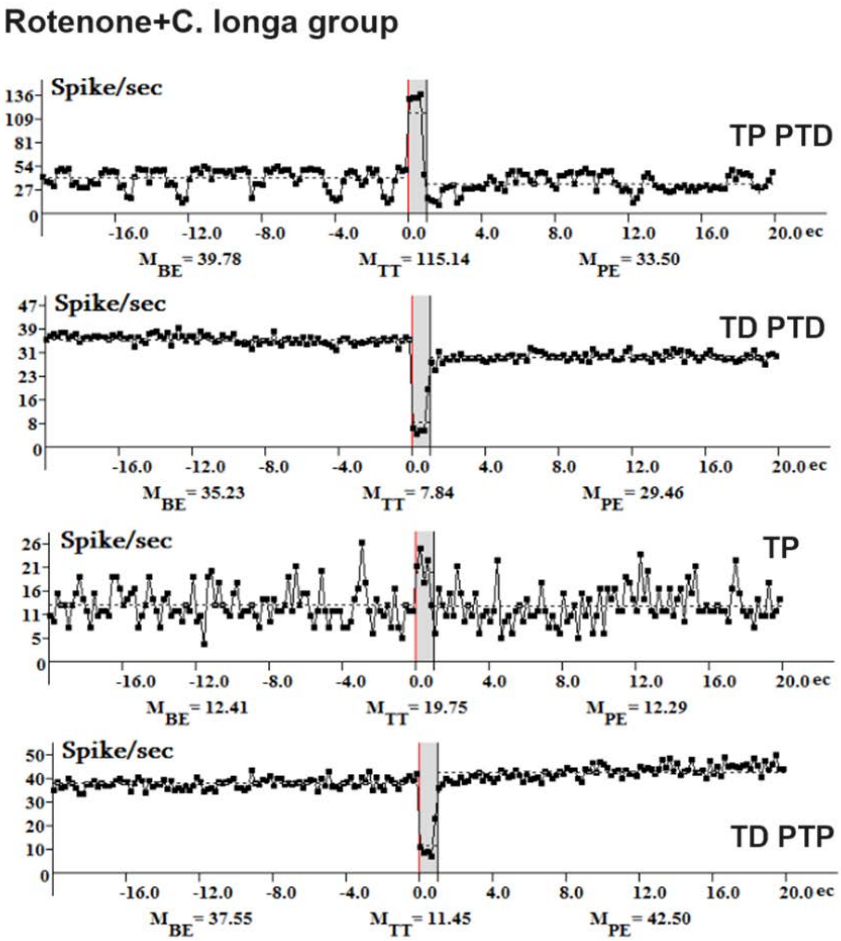

Figure 4. *Effects of C. longa on hippocampal neuronal activity. Examples of spike activity in a single neuron include real-time impulse flow 20 sec before (BE, before the event) and 20 sec after stimulation (PE, post-event).*

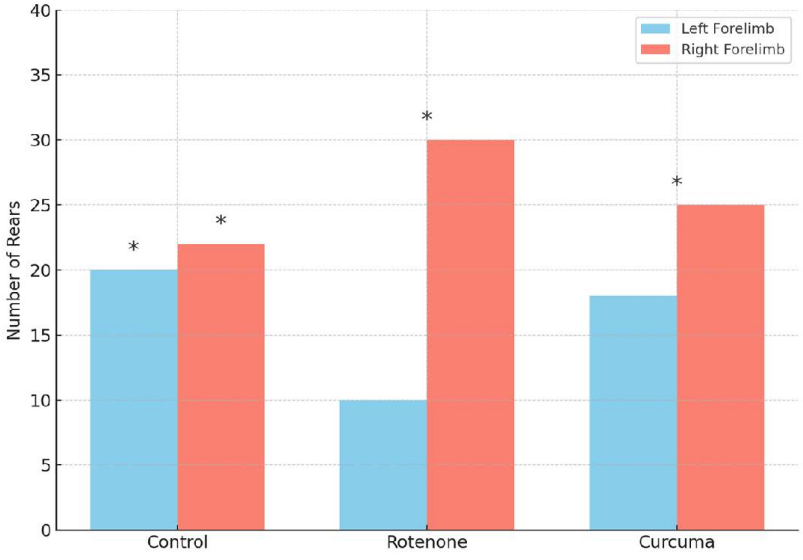

Figure 5. *Effect of Curcuma on the number of rears in the Cylinder test.*

control group. The higher percentage of TP PTP responses in the Curcuma group also suggests an enhancement of stimulatory neural activity, which could contribute to improved motor and cognitive function. This increase in stimulatory responses, combined with the significant increase in TP PTD responses, may reflect a protective mechanism against the degenerative changes induced by rotenone in the PD model. The observed distribution of TD, TD PTP, TP PTD, TP PTP, and TP responses in the Curcuma group indicates a complex modulation of hippocampal neuronal activity, potentially involving multiple pathways affected by *Curcuma longa* supplementation. These results warrant further investigation into the specific mechanisms underlying *Curcuma longa's* neuroprotective effects in PD and its potential as a therapeutic intervention for mitigating PD-related neurodegeneration.

In our cylinder test results, the significant interaction effect suggests that the impact of the treatment group on the number of rears varies depending on the forelimb, indicating differential effects of treatment on motor behavior. The cylinder test is a reliable and objective assay of brain function that can evaluate rodent's spontaneous forelimb use, which is the main advantage of this test [29]. It has been used in a number of motor system injury models of stroke and can detect even mild neurological impairments [21]. These motor deficits are typically associated with nigrostriatal dopaminergic neuron loss and impaired motor control [30]. Curcuma treatment did not significantly improve the number of rears compared to Rotenone alone, suggesting partial or limited neuroprotective efficacy under the present experimental conditions. Curcumin, the active component of *Curcuma longa*, has been reported to exert antioxidant, anti-inflammatory, and neuroprotective effects in various neurodegenerative models, including PD [30,31]. The significant interaction and post-hoc analyses revealed forelimb asymmetry in the Rotenone and Curcuma groups but not in controls, indicating lateralized motor impairments. This asymmetry is a hallmark of unilateral or asymmetric nigrostriatal lesions and is well-documented in rodent PD models [32]. Forelimb-specific deficits are critical for assessing the extent and progression of motor dysfunction and for evaluating therapeutic interventions [33]. These findings underscore the importance of analyzing lateralized motor behaviors in preclinical models of PD, as they reflect the pathophysiological asymmetry observed in patients [34]. Moreover, the Cylinder test remains a sensitive and reliable assay for detecting subtle motor impairments and recovery following neurotoxic insult or treatment [35].

Conclusion.

Overall, our study underscores the potential neuroprotective effects of *Curcuma longa* in PD and emphasizes the need for further research to elucidate the specific mechanisms underlying its benefits. *Curcuma longa* holds promise as a therapeutic intervention for PD-related neurodegeneration and warrants continued investigation for its clinical application in PD management.

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Competing interest.

The authors declare that they have no conflict of interest.

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Data availability.

The data underlying this article will be shared on reasonable request to the corresponding author.

Ethical statement.

The experimental procedures followed the guidelines outlined in the European Communities Council Directive (2010/63/UE) and were approved by the Ethics Committee of the Yerevan State Medical University after Mkhitar Heratsi (Approval code: N4 IRB APPROVAL, November 15, 2018).

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