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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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MORPHOHISTOCHEMICAL ANALYSIS OF CORTICAL STRUCTURES IN AN EXPERIMENTAL MODEL OF PROLONGED COMPRESSION SYNDROME OF THE HIND LIMB IN RATS

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Abstract.

Crush syndrome (CS) is a pathological shock-like condition that develops following prolonged compression of the trunk, extremities, or their segments by heavy objects, and is characterized by an inflammatory response that extends beyond the affected soft tissues and penetrates into complex brain structures. To investigate the dynamics of the morphological and functional state of rat brain cellular structures following hind limb compression, we employed a histochemical method for detecting the activity of Ca^{2+}-dependent acid phosphatase. Experiments were performed on sexually mature albino rats. Experimental CS models were created using a custom apparatus that allowed 3-hour and 6-hour compression of the hind limb soft tissues. Morphohistochemical analysis revealed that after 3 hours of compression, neurons in the sensorimotor cortex (SMC) largely retained their typical morphology, dendritic orientation, and moderate levels of cytoplasmic enzymatic activity. In a subset of neurons—predominantly in the granular layer—early signs of central chromatolysis were observed. After 6 hours of compression, the morphological profile of neurons in the studied SMC layers deteriorated markedly: alterations in cell shape and size, neuronal deformation, nuclear ectopia, and shortened or disrupted neurites indicated impaired intercellular connectivity. Notably, pyramidal neurons exhibited greater resilience compared with granular cells. An increase in nuclear acid phosphatase activity suggests the activation of early preventive mechanisms of the cellular damage response during the initial stages of injury. Thus, Ca^{2+}-dependent acid phosphatase histochemistry demonstrated that crush syndrome is accompanied by progressive morphological impairments in SMC neurons, which become more pronounced with increasing compression duration. The observed morphological features of SMC neuronal injury following limb compression are characteristic of nonspecific neuronal damage and resemble acute neuronal swelling—a common, reversible form of cellular pathology. which is recognized as a reversible alteration.

Key words. Crush syndrome, prolonged compression syndrome, sensorimotor cortex, Ca^{2+}-dependent acid phosphatase, neuronal morphology.

Introduction.

Over the past decades, crush syndrome (CS) has gained increasing clinical and research relevance due to the rising frequency of natural disasters, industrial and motor vehicle accidents, armed conflicts, and the persistence of numerous unresolved and debated aspects of its pathogenesis. CS is a severe pathological condition resulting from closed injury to large areas of soft tissue under the influence of substantial and/or prolonged mechanical force. It is accompanied by a constellation of specific pathological disturbances, including shock, cardiac rhythm disorders, acute renal failure, and compartment syndrome [1-3]. The syndrome typically develops upon the sudden release of sustained pressure on muscles and bones, triggering a massive systemic response. Damaged muscle tissue releases myoglobin, potassium, creatine kinase, uric acid, phosphorus, and proteolytic enzymes into the bloodstream, leading to electrolyte imbalance, oxidative stress, and direct injury to renal tubular cells [4,5]. The severity of the clinical course is directly correlated with both the duration of compression and the extent of tissue damage. Based on these parameters, three degrees of severity are distinguished. Mild CS develops after relatively short periods of compression (2–3 hours) and, with appropriate treatment, carries a favorable prognosis. Moderate CS occurs when compression lasts up to 6 hours, is associated with endotoxemia and renal dysfunction, and its prognosis depends on the timeliness and quality of first aid, as well as subsequent management with early implementation of extracorporeal detoxification. Severe CS arises following compression exceeding 6 hours, is characterized by rapidly escalating endogenous intoxication, and leads to life-threatening complications. Without prompt, intensive treatment, the prognosis is poor [6]. Although the primary initiating factor in CS is mechanical compression of a body segment, the pathological cascade is predominantly driven by three interrelated mechanisms: toxemia, hypovolemia, and pain. Toxemia results from the entry of degradation products of damaged tissues into the systemic circulation, exerting profound toxic effects and disrupting homeostasis. Prolonged ischemia triggers a shift to anaerobic metabolism and initiates structural degradation of tissues, while subsequent reperfusion induces the generation of reactive oxygen species, the release of inflammatory mediators, and an increase in vascular permeability. These processes promote the redistribution of fluid into the “third space” (third-spacing), leading to marked hypovolemia and, in the absence of timely intensive care, may progress to shock and multiple organ failure [4,7]. In patients whose resuscitation is delayed, symptoms may include nausea, vomiting, agitation, and delirium [8].

In the pathogenesis of crush syndrome (CS), pain serves as a primary triggering factor during compression and crushing injuries, although it is often absent in cases of positional compression where consciousness is impaired or lost. Pain is particularly pronounced in limb compression injuries, where a dense network of nociceptors in the skin, skeletal muscles, and periosteum is activated. Through neuro-reflex pathways, nociceptive input stimulates both cortical and subcortical

centers of the brain, mobilizing diverse protective systems of the organism—including conscious perception, sensory processing, autonomic regulation, behavioral adjustments, and somatic responses [9,10]. With prolonged compression, pain intensity may diminish, masking profound underlying metabolic disturbances. Pain itself disrupts central nervous system function by impairing the balance between excitatory and inhibitory processes. In compression trauma, the excitatory phase is often sustained, a phenomenon attributed to the absence of significant blood loss and preserved cerebral perfusion. The erectile phase of shock may persist for approximately 1.5 hours before transitioning into the torpid phase. Immediately after decompression, a brief period of excitation is often observed—a phenomenon referred to as the "second hit" or "additional strike." This is followed by renewed inhibition, manifesting as deeper impairments in the function of vital organs [11].

Prolonged nociceptive stimulation, mediated via the central nervous system, induces complex humoral alterations in the body—oxidative–reductive processes are suppressed, gas exchange and the physicochemical properties of blood are impaired, adrenal activity is enhanced, and adrenocorticotropic hormone (ACTH) secretion is stimulated, in turn promoting catecholamine release. This cascade is accompanied by spasm of arterioles and precapillary sphincters within the microcirculatory network. Due to oxygen deficiency, incompletely oxidized metabolic products accumulate in tissues, leading to metabolic acidosis and a marked increase in the concentration of vasoactive mediators [12]. Recent research has focused on advanced biomaterials—such as hydrogels and nanofibrous matrices—capable of sustaining regenerative signaling at sites of injury [13]. Neuronal activity itself also exerts a profound influence on recovery. Properly timed sensory input can enhance motor neuron sprouting and accelerate functional restitution. Within the spinal cord, mechanisms such as presynaptic depolarization of afferents and presynaptic inhibition modulate signal transmission and can restore the balance of sensorimotor circuits after injury [14]. Thus, crush syndrome should not be viewed solely as a muscular or renal injury, but rather as a complex, multisystem crisis. Understanding the interplay among ischemic injury, toxemia, glial transformation, neurotrophic signaling, and synaptic remodeling forms the foundation for integrated therapeutic strategies aimed at preserving life and restoring function.

Over the past decade, numerous animal studies have employed models simulating crush syndrome (CS), yielding promising results. The scientific literature contains reports on histological and ultrastructural alterations in the heart, kidneys, liver, lungs, skeletal muscles, and loose connective tissue across various organs in experimental CS [7,15-17]. The time course of oxidative damage in different brain regions was investigated in the gerbil model of transient cerebral ischemia, and provide further evidence that oxidative stress may be involved in delayed neuronal death in gerbils [18]. However, there is a notable absence of data addressing changes in the cellular structures of the brain under experimental CS, particularly in cases accompanied by systemic shock. Of particular importance is the morphofunctional status of the cellular structures of the sensorimotor cortex, which is responsible for processing sensory information and controlling motor functions. This cortical region plays a central role in integrating sensory modalities—including touch, temperature, pain, and proprioception—with motor control, thereby enabling environmental adaptation and the execution of goal-directed behaviors.

In light of these considerations, the aim of the present study was to investigate the morphofunctional state of the sensorimotor cortex in the cerebral hemispheres of rats following 3-hour and 6-hour compression of the hind limb soft tissues.

Materials and Methods.

Animals:

Experiments were conducted on sexually mature male albino rats (mean body weight: 200 ± 30 g), obtained from the Experimental Center of the L.A. Orbeli Institute of Physiology, National Academy of Sciences of Armenia. Animals were housed under standard laboratory conditions, with a 12-hour light/dark cycle, ambient temperature maintained at 22–24°C, and relative humidity of 40–60%. They were provided ad libitum access to standard pelleted chow (Nutrimix STD-1020) and filtered tap water. Drinking water was routinely tested for potential contaminants to ensure compliance with established laboratory quality standards.

Experimental Model:

The experimental model of crush syndrome (CS) was established using a custom-built apparatus designed to apply localized compression to one pelvic limb. This model was reproduced on a specially engineered device developed for investigating various aspects of the pathogenesis and treatment of CS (Rationalization Proposal No. 158, 10.06.1990, issued by Yerevan Medical Institute) [19]. The apparatus, designed by the staff of the YMI Research Center, consists of two test compartments of equal volume, separated by a thin partition. One compartment contains a compression mechanism, mirrored by an identical unit in the second compartment. The system allows for controlled, uniform application and release of pressure to the limbs of small laboratory animals (rats, mice), with the applied force recorded on a dynamometer. The compression element is a circular plate with a diameter of 2 cm. In this study, a pressure of 140 kPa was applied to an area of 3.14 cm^2.

Two models of crush syndrome (CS) were established to represent different degrees of severity: compression of a single limb for 3 hours (CS3 group) to model a mild form of CS, and compression of a single limb for 6 hours (CS6 group) to model a moderate form. The affected area encompassed the entire inner surface of the thigh (3.14 cm^2). Control animals were placed in the apparatus for the same duration but without any applied load. Following the release of compression, decompression was performed over a 1-hour period. Animals were then euthanized under deep anesthesia with sodium pentobarbital (100 mg/kg, intraperitoneally) to harvest the brain for histochemical analysis.

Study Design:

Fifteen rats were randomly assigned to three experimental groups, each containing five animals:

Control group (Co): no intervention;

CS3 group: rats subjected to hind limb compression for 3 hours;

CS6 group: rats subjected to hind limb compression for 6 hours.

The number of animals per group (n = 5) was determined in accordance with the 3R principles (Replacement, Reduction, Refinement).

Histochemistry study:

In the present study, we employed a histochemical technique for detecting Ca^{2+}-dependent acid phosphatase (AP) activity, originally described by Meliksetyan [20,21]. This method integrates elements of traditional Nissl staining and Golgi silver impregnation, enabling simultaneous visualization of neuronal cytoarchitecture and enzyme distribution patterns. Enzymes in living organisms act as biocatalysts, facilitating metabolic reactions through active centers that convert specific substrates [22]. The methodological approach is based on detecting intracellular phosphorus-containing compounds crucial for energetic processes involved in maintaining and reproducing vital systems. When acid phosphatase activity is tested, phosphate ions released by the enzyme react with various structures in the mixture, regardless of their spatial arrangement. After incubation in a sodium sulfide solution, these ions form a visible dark brown precipitate of lead sulfide. This staining provides a clear and informative image, allowing for detailed analysis of specific metabolic pathways within the examined structures.

Experimental procedure:

Following confirmation of death, brains were carefully removed and fixed in a 5% neutral formalin solution prepared in 0.1 M phosphate buffer (PBS, pH 7.4) for 48 h at +4 °C. Frontal-plane sections of the target brain regions were cut at a thickness of 50–60 μm using a cryostat microtome (YD-2235, Jinhua YIDI Medical Appliance Co., Ltd., China).Sections were transferred to freshly prepared incubation medium for Ca^{2+}-dependent AP detection, containing 0.4% lead acetate, 1 M acetate buffer (pH 5.6), and 2% sodium glycerophosphate. Incubation was carried out in a thermostat at 37°C for 1.5 h. After incubation, sections were rinsed in distilled water, developed in sodium sulfate solution, rinsed again, and mounted in Canada balsam (VWR Chemicals, Canada). Morphological assessment was performed under a light microscope. Topographical identification of brain structures was guided by established atlases [23,24]. Microphotographs were acquired using an OPTON M-35 microscope (West Germany) equipped with an AmScope MU800 digital camera.

Results.

Analysis of the morphohistochemical data from rat brains following hind limb compression revealed that the sensorimotor cortex (SMC) is the most severely affected region. Due to this selective vulnerability, the study focused on this area of the cerebral cortex. A detailed assessment of the distribution of lesions, both across the cortical surface and in depth, demonstrated that the pyramidal layers (Figure 1 C–F; Figure 2 C–F) and the outer granular layer (Figure 3 C–F) of the SMC were most frequently affected.

Morphohistochemical analysis further showed that after 3 hours of hind limb compression (CS3 group), neurons in the inner pyramidal layer of the cortex were predominantly pyramidal cells with correctly oriented apical dendrites, exhibiting high acid phosphatase activity and large granular deposits in the cytoplasm and apical dendrites. Granulation was so pronounced that neuronal nuclei were often not visible. These neurons were slightly enlarged compared to controls, yet retained their overall shape and dendritic architecture (Figure 1 C, D).

A frequent observation was the contrast between the intensity of chromatolysis and the preserved structural integrity of some neurons, likely reflecting intrinsic neuronal resistance. In certain large pyramidal cells, the nuclei appeared pale and centrally located, with clearly traceable apical dendrites and high enzymatic activity in both the cytoplasm and dendritic processes (Figure 1 C). In these cells, acid phosphatase deposits were distributed homogeneously. Amid these relatively preserved neurons, occasional pyramidal cells exhibited pathological changes. These neurons appeared swollen, with shortened or unresponsive dendrites, indistinct contours, although the overall cell shape remained intact. The pattern of neuronal injury resembled central chromatolysis; however, chromatolysis was not the predominant feature. Additionally, some neurons lost their characteristic morphology entirely: cells became rounded, dendrites were absent, contours were blurred, and nuclei were displaced toward the periphery (Figure 1 C, D). Similar alterations were observed in the outer granular layer of the SMC (Figure 3 C, D).

In the outer pyramidal layer, no significant alterations were observed; neuronal contours remained well-defined, with moderately expressed enzymatic activity (Figure 2 C, D). Intracellular granulation was clearly evident. These neurons retained their size, shape, and dendritic processes, with only occasional cells exhibiting shortened processes. The lightly stained nuclei were centrally located, similar to those in control (Co) animals. Compared to normal conditions, enzymatic activity in neurons of the outer pyramidal layer was increased, indicating elevated metabolic activity and heightened neuronal function following 3 hours of hind limb compression.

In the outer granular layer of the sensorimotor cortex (SMC) of CS3 group animals, neurons exhibited pronounced chromatolysis (Figure 3 D). Lead phosphate deposits in the cytoplasm were fine-granular. These neurons were markedly enlarged, hypertrophied, and deformed, with non-responsive dendritic processes. In the cytoplasm of hypertrophied neurons, granular deposits in the central region disappeared, and the cells assumed a rounded shape, with the cell membrane highlighted by a thin submembranous layer of precipitate. Within these structures, a large, swollen, lightly stained nucleus was typically observed centrally, containing a darkly stained nucleolus (Figure 3 C, D).

Dendritic processes were absent in these granular neurons, indicating disruption of intercellular contacts within this cortical layer. The morphological pattern resembled acute neuronal swelling, a relatively common form of cellular pathology. Amid these severely affected neurons, some cells retained normal morphology, preserved dendritic processes, and exhibited high phosphatase activity (Figure 3 C, D).

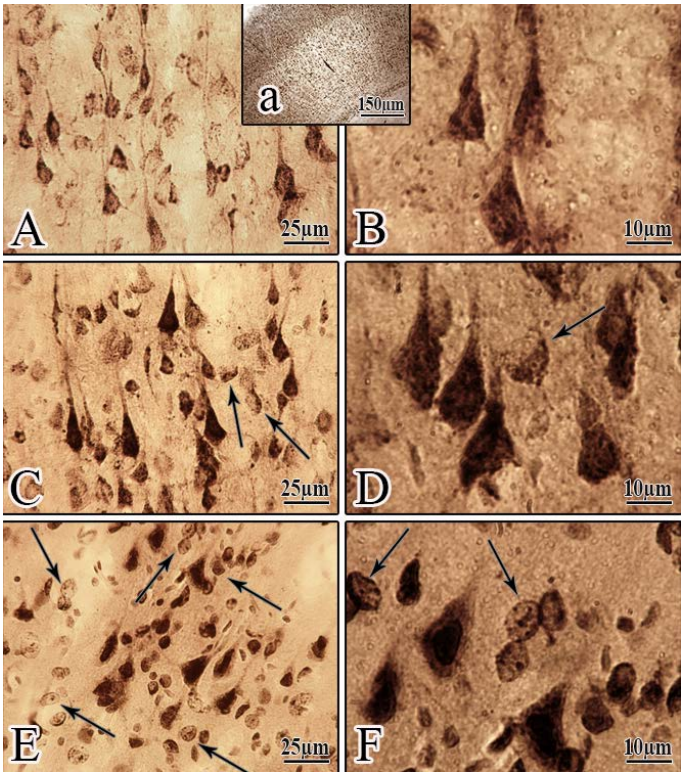

Figure 1. *Micrographs of neurons in the inner pyramidal layer of the rat sensorimotor cortex under normal conditions (A, B), after 3-hour (C, D) and 6-hour (E, F) hind limb compression. Black arrows indicate central chromatolysis; a denotes all cortical layers. Panels C and D show neurons characterized by increased cytoplasmic acid phosphatase activity; panels E and F depict hyperactivation of nuclei in neurons of the inner pyramidal layer. Detection of Ca^{2+}-dependent acid phosphatase activity. Magnification: ×63 (a); ×400 (A, C, E); ×1000 (B, D, F).*

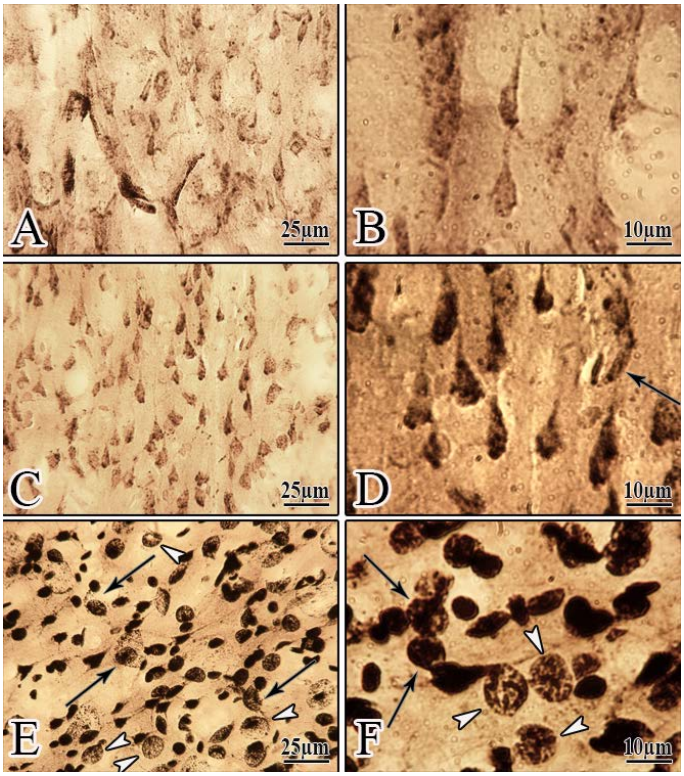

Figure 2. *Micrographs of neurons in the outer pyramidal layer of the rat sensorimotor cortex under normal conditions (A, B), after 3-hour (C, D) and 6-hour (E, F) hind limb compression. Panels C–F show neurons characterized by increased cytoplasmic acid phosphatase activity, with activation particularly pronounced after 6 hours of compression. Black arrows indicate central chromatolysis; arrowheads denote submembranous localization of acid phosphatase with ectopic nuclei. Detection of Ca^{2+}-dependent acid phosphatase activity. Magnification: ×400 (A, C, E); ×1000 (B, D, F).*

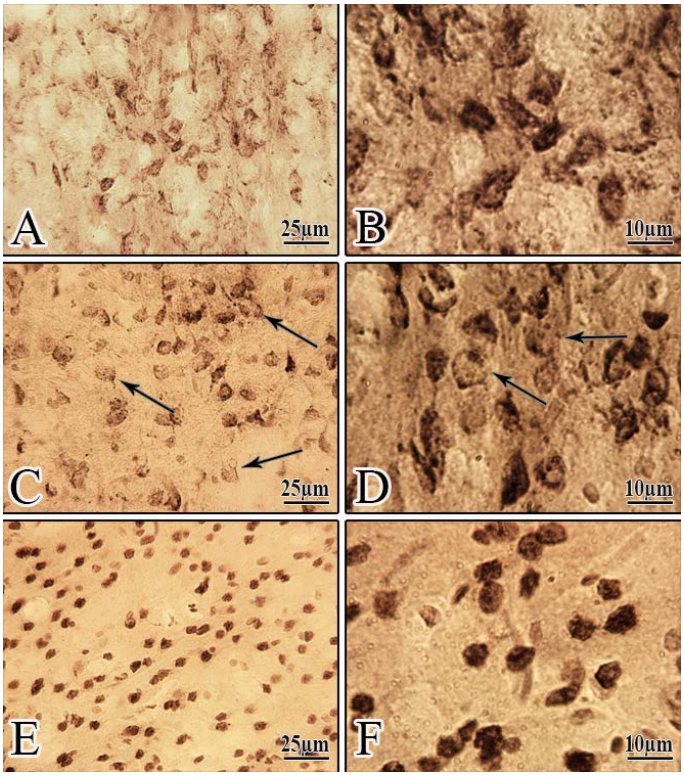

Figure 3. *Micrographs of neurons in the outer granular layer of the rat sensorimotor cortex under normal conditions (A, B), after 3-hour (C, D) and 6-hour (E, F) hind limb compression. Panels E and F show shrunken neurons characterized by increased cytoplasmic acid phosphatase activity. Black arrows indicate central chromatolysis. Detection of Ca^{2+}-dependent acid phosphatase activity. Magnification: ×400 (A, C, E); ×1000 (B, D, F).*

The morphological profile of the sensorimotor cortex (SMC) following 6-hour hind limb compression (CS6 group) demonstrates a deepening of cellular damage across its various layers. While 3-hour compression primarily induced moderate alterations in neuronal structural properties and increased phosphatase activity in neurons of the studied layers, 6-hour compression led to changes characteristic of primary neuronal irritation, placing cells on a trajectory toward substantial injury. At this stage, acid phosphatase activity was markedly elevated across all cortical layers. Neurons appeared intensely stained due to high phosphatase activity, likely reflecting mobilization of intrinsic protective mechanisms and the activation of cellular adaptive responses.

In the inner pyramidal layer of the SMC (Figure 1 E, F), intensely stained, hypertrophied neurons were observed, with disrupted polarity of the apical dendrites: some neurons retained the correct radial orientation of the apical dendrite, whereas others were tilted, fully inverted, or oriented perpendicularly to the inner granular layer (Figure 1 E). Compared to the control group, phosphatase activity in both the cytoplasm and nucleus was increased, indicating activation of metabolic processes aimed at maintaining homeostasis disrupted by the applied stress. Cells with severe damage were also identified. These neurons lost their characteristic morphology and became rounded, with blurred contours, pale cytoplasm, and sparse granular deposits in the soma. In this state, the cells were swollen and hypertrophied, with most dendritic processes non-responsive (Figure 1 E). Nuclei were similarly swollen and displaced toward the periphery, often localizing to one pole of the cell. Occasionally, hypertrophied neurons affected by chromatolysis were observed, with swollen nuclei centrally positioned and surrounded by a thin layer of fine granular lead phosphate precipitate (Figure 1 E).

Following 6-hour hind limb compression, the outer pyramidal layer of the SMC exhibited pronounced degenerative changes. Neurons of varying shapes and sizes (oval, elongated) were deformed, sometimes clustered, and partially or completely devoid of dendritic processes. Neuronal injury was associated with disorganization of normal tissue architecture, and phosphatase activity was markedly elevated (Figure 2 E, F). In some cells, the cytoplasm was so intensely stained that nuclei were difficult to distinguish from the surrounding cytoplasm (Figure 2 E, F), indicating a hyperactive neuronal state. Neuronal damage in the outer pyramidal layer followed the pattern of central chromatolysis. Most pyramidal cells were severely affected, losing their characteristic shape and hypertrophying; some became rounded, and dendritic processes were largely unresponsive. Swollen nuclei were displaced toward the periphery, localizing to one pole of the cell in an eccentric position. In the cytoplasm of swollen neurons lacking processes, granular precipitates disappeared, and cells assumed a spherical appearance, outlined by a thin layer of deposit. In these neurons, the thick, radially oriented apical dendrite was no longer identifiable (Figure 2 E). In individual cells, profound damage was observed, manifested as progressive dissolution of the Nissl substance, beginning centrally. The swollen, lightly stained nuclei remained centrally located, with cell membranes clearly delineated by a surrounding layer of dark

granular precipitate (Figure 2 F). A frequent observation was the discrepancy between the intensity of chromatolysis and the preserved structural integrity of some neurons, likely reflecting intrinsic neuronal resistance. Thus, immediately following 6-hour hind limb compression, the outer pyramidal layer of the cortex displayed neurons with varying degrees of cellular damage.

Amid these damaged neurons, some cells retained relatively normal morphology and exhibited high phosphatase activity, with apical dendrites maintaining proper vertical orientation. These neurons were enlarged and hypertrophied but preserved their characteristic shape; the cell membrane was well-defined, with intensely stained contours, and dendritic processes remained responsive over considerable distances from the soma. The trajectory of dendrites was clearly traceable, showing punctate granulations. High phosphatase activity was evident in the cytoplasm of these pyramidal neurons (Figure 2 E), indicated by intense basophilic staining, reflecting enhanced phosphorylation and increased metabolic activity. In the outer granular layer, alongside some neurons with preserved morphology, most cells were shrunken, homogeneously stained, and had lost their characteristic form (Figure 3 E). These neurons exhibited reduced cell body size and hyperchromatosis, indicative of elevated phosphatase activity, and assumed elongated, rounded, or curved shapes. In these shrunken granular neurons, nuclei were centrally located with darkly stained nucleoli. Dendrites were thinned and shortened. In some instances, granular cells appeared as large, hyperphosphorylated, structureless formations (Figure 3 F).

Discussion.

The results of the present study of the rat brain following hind limb compression demonstrated neuronal tissue damage primarily affecting the neurons and their processes. The morphological pattern of neurodegenerative changes in the cerebral cortex was characterized by discontinuous distribution, with some cortical regions exhibiting more pronounced lesions while others remained intact. The sensorimotor cortex was the most severely affected; therefore, due to its selective vulnerability, morphohistochemical analyses were focused on this region of the cerebral cortex. Analysis of the spatial distribution of lesions, both along the cortical surface and through its depth, revealed that the outer granular layer, as well as the inner and outer pyramidal layers, were the most frequently affected. The morphological changes observed in pyramidal layers of the SMC following hind limb compression represent an adaptive response to diverse pathological insults, are characteristic of non-specific neuronal injury, and predominantly resemble acute neuronal swelling—a common and reversible form of cellular pathology. As our study did not include an evaluation of animals during the recovery phase following hind limb compression in rats, we are unable to determine whether the observed cellular changes are reversible. This should be acknowledged as a limitation of the present work. The number of animals in each group (n = 5) was chosen according to the 3R (Replacement, Reduction, Refinement) principles, which may not be enough to provide statistical power for qualitative analysis, and this is also a limitation of this study.

After 3-hour of hind limb compression in rats, no substantial differences were observed in the response of cortical neurons compared to controls, with the exception of neurons in the granular layer. Within the pyramidal layers, only occasional neurons displayed signs of central chromatolysis. In contrast, the outer granular layer showed a predominance of neurons undergoing marked chromatolysis. The most pronounced alterations emerged after six hours of compression. In the majority of cortical neurons, dendritic processes ceased to respond; however, some cells—particularly within the pyramidal layers—retained their processes, albeit with distorted orientation of the apical dendrite. In the pyramidal layers of the cortex, hypertrophied neurons with severe structural damage were identified. The outer granular layer exhibited evidence of neuronal shrinkage accompanied by abnormal shape and size. Furthermore, a reduction in dendritic arborization was noted, suggesting impaired inter-neuronal connectivity—an early hallmark of cortical pathology. Among neurons affected by chromatolysis, a subset demonstrated intense acid phosphatase activity within both cytoplasm and nucleus. These cells preserved their morphology and processes but displayed swelling, indicating an early stage of degenerative change

Immediately following 6 hours of hind limb compression, neurons within both the pyramidal and granular layers of the sensorimotor cortex (SMC) exhibited markedly elevated Ca^{2+}-dependent phosphatase activity, likely reflecting an adaptive response aimed at preserving cellular viability. This increase indicates active phosphorylation, representing one of the transcriptional pathways preceding the production of stress-responsive peptides [25,26].

The morphological and physiological disturbances observed in neurons of both the inner and outer layers of the SMC, particularly involving the cytoplasm–nucleus relationship and associated with alterations in cellular respiration and enzymatic function, were occasionally manifested immediately after compression as nuclear distress. This was accompanied by adaptive displacement of the nucleus toward the neuronal periphery, suggesting an early protective cellular mechanism [27].

Conclusion.

The present study demonstrates that prolonged compression syndrome (PCS), in addition to affecting classical target organs such as the site of compression, kidneys, liver, and several other organs, also impacts the sensorimotor cortex (SMC) of the rat brain. PCS is accompanied by pain and stress-related factors, which indirectly influence multiple brain regions, altering their function and activity. Our findings indicate that neuronal damage occurs across all layers of the SMC at both compression durations, manifesting primarily as central chromatolysis to varying degrees. Neurons of the granular layer are particularly affected, exhibiting pronounced shrinkage. The morphological characteristics observed resemble acute swelling, which is recognized as a reversible alteration. Understanding the cerebral response to PCS is essential for guiding clinical interventions in affected individuals, particularly to prevent the involvement of cortical regions in the pathological processes that unfold during the decompression period.

Author contributions.

Study Concept and Design: IAS and DMH. Acquisition, Analysis, and Interpretation of the Data: IAS, DMH, AIV, ANH, MAA, KKV and NKA. All of the authors have contributed substantially to the manuscript.

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Availability of data and materials.

Raw data can be provided upon request to the corresponding author.

Declarations.

Competing interests. The authors declare no competing interests.

Conflict of interest. The authors declare no conflict of interest.

Ethical approval and consent to participate.

The experimental protocol corresponded to the conditions of the European Communities Council Directive (2010/63/ UE) and the "ARRIVE" guidelines (Animals in Research: Reporting In Vivo Experiments). The protocol was approved by the Institutional Review Board of the L. A. Orbeli Institute of Physiology (protocol code: N4, approval date: July 22, 2021).

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МОРФОГИСТОХИМИЧЕСКИЙ АНАЛИЗ КОРКОВЫХ СТРУКТУР В ЭКСПЕРИМЕНТАЛЬНОЙ МОДЕЛИ СИНДРОМА ДЛИТЕЛЬНОГО СДАВЛЕНИЯ ЗАДНЕЙ КОНЕЧНОСТИ У КРЫС

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Резюме

Синдром длительного сдавления (СС) представляет собой патологическое шокоподобное состояние, наступающее после длительного сдавления туловища, конечностей или их сегментов тяжелыми предметами, и характеризующееся воспалительной реакцией, которая выходит за пределы мягких тканей и проникает в сложные структуры головного мозга. С целью изучения динамики морфофункционального состояния клеточных структур головного мозга крыс после сдавления задней конечности был применён гистохимический метод выявления активности Ca^{2+}–зависимой кислой фосфатазы. Исследования проводили на половозрелых крысах Альбино. На специальной установке были созданы экспериментальные модели СДС в условиях 3-х и 6-и часовой компрессии мягких тканей задней конечности крыс. Результаты морфогистохимического анализа показали, что после 3-х часа компрессии нейроны СМК в основном сохраняли морфологическую картину, характерную ориентацию дендритов и умеренный уровень ферментативной активности в цитоплазме. У части клеток отмечались ранние признаки центрального хроматолиза, в основном в зернистом слое коры. После 6 часов компрессии морфологическая картина нейронов изучаемых слоев СМК значительно ухудшалась: нарушение формы и размеров клеток, деформированные нейроны, эктопированные ядра, перерванные и укороченные отростки, что указывает на нарушение межклеточной связи. Примечательно, что пирамидные нейроны демонстрировали большую устойчивость по сравнению с зернистыми клетками. Выявленное повышение ядерной активности кислой фосфатазы свидетельствует о включении ранних превентивных механизмов клеточного ответа на повреждение уже в начальных стадиях травмы. Таким образом, методом выявления активности Ca2+-зависимой КФ показано, что синдром длительного сдавливания сопровождается нарушениями морфологической картины нейронов СМК, которые углубляются при увеличении длительности компрессии. Морфологическая картина повреждений, наблюдаемых в СМК после сдавливания конечности, присуща неспецифическим нейрональным поражениям и напоминает острое набухание нервных клеток, которое относится к довольно распространенному виду клеточной патологии, который распознается как обратимое изменение.

Ключевые слова: краш-синдром, синдром длительного сдавления, сенсомоторная кора, Ca^{2+}-зависимая кислотная фосфатаза, морфология нейронов.