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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 ВИНТИ 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 ВИНТИ 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. Корректур авторам не высылаются, 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 computer-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 საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ 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, ანათალებების შედეგების 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 ფხიხლებში 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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IMPROVEMENT OF COGNITIVE FUNCTION IN WISTAR RATS UNDER CHRONIC STRESS CONDITIONS WITH MELATONIN

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Abstract.

Stress is a significant factor affecting cognitive functions such as memory, attention and learning ability. This paper examined the effects of melatonin at different dosages on cognitive performance compared to choline alfoscerate on wistar line rats under chronic stress conditions. The studied rats were subjected to stress - Porsolt's forced swim test.

Before and after the stress test, blood was collected from the tail vein of the rats. Cortisol levels increased in all groups, including the control group. However, the melatonin levels in each group changed to a different degree as each group was offered different levels of melatonin dosage and the drug, choline alfoscerate.

In the result, it was found that rats receiving low doses of melatonin did not improve the results, increasing the time from 29.7 to 38.2 seconds. The rats receiving high doses of melatonin performed the best, with virtually no increase in time to complete the maze (increasing the time from 29.6 to 33.5 seconds). The group receiving choline alfoscerate showed similar results to the control group, significantly increasing the maze time from 29.4 to 47.4 seconds.

Key words. Stress, melatonin, memory, attention, epiphysis.

Introduction.

In the modern world, stress has become an integral part of every person's life. Given the fast pace of life, high demands at work, social and economic changes, stressful situations arise almost daily. Chronic stress not only impairs the quality of life, but also leads to serious health consequences, including cardiovascular diseases, gastrointestinal disorders and weakening of the immune system [1-3].

Stress is a significant factor affecting cognitive functions such as memory, attention and learning ability [1].

Stress can be defined as a state of anxiety or mental tension caused by a difficult situation. At the same time, it is a natural human reaction that focuses the attention on the problems or threats encountered in daily life.

There are many endogenous products that protect the body from the excessive-unwanted effects of stress-releasing systems. One of these is melatonin. It is an antagonist of the stress hormone cortisol, in chronic stress it protects against its damaging effects.

Studies show that melatonin can not only help improve sleep, but also have a positive effect on memory, attention and general psycho-emotional state, which makes it a potential remedy for people suffering from chronic stress [4,5].

In humans, the light cycle is perceived by the retina of the eye, then the nerve signal through the retino-hypothalamic tract goes to the suprachiasmatic nuclei of the hypothalamus, and then to the upper cervical ganglion.

From the upper cervical ganglion, information about light

comes to the epiphysis: it is mediated by norepinephrine, which is released by nerve endings directly into the parenchyma (pinealocytes) of the epiphysis, which eventually leads to the start of melatonin synthesis. Melatonin synthesis effectively occurs only with the onset of darkness and decreases in the light phase of the day [4]. Since people with chronic stress often lack normal sleep, they are deficient in endogenous melatonin.

In this article we will review the mechanisms of melatonin's effect on cognitive function and its potential use as a remedy for chronic stress in comparison with other medications.

Purpose of the study: to compare the effects of low and high doses of melatonin and choline alfoscerate on cognitive functions in stressed Wistar rats.

Materials and Methods.

The object of the study was Wistar rats (n=80), which were bred for research work. The rats were placed in special cages and were kept in a laboratory box in which the conditions necessary for their habitat were constantly maintained: moderate lighting, air humidity 30-50% at a temperature of 18-20°C, use of exhaust ventilation system. Four groups were formed: control group, which did not receive the drugs (n=20), experimental group № 1, which received low doses of melatonin 1mg/kg body weight (n=20), experimental group № 2, which received high doses of melatonin 10 mg/kg body weight (n=20), experimental group № 3, which received choline alfoscerate 25 mg/kg (n=20).

The studied rats were subjected to stress - Porsolt's forced swim test.

The 12 h/12 h light day was strictly observed for the experiment.

Results and Discussion.

The studies were performed on 80 male Wistar rats weighing 200-250 g.

Before the onset of stress, the rats were placed in a Morris water maze. This maze allowed to estimate their motor activity and to create homogeneous groups of animals with the same constitutional features.

The Morris water maze was used as a method of identification and distribution of rats into groups.

The Morris Water Maze is used in scientific research to study spatial memory and learning in animals.

A plastic container with transparent walls, 150 cm long and 60 cm wide, was used to create the Morris Water Maze. The platform was a piece of plastic attached to the wall with suction cups. The tracking system was a stopwatch.

This method provided information about the cognitive abilities of rats before and after excrement.

Before starting the experiment, the container was filled with water to a level that allowed the rats to swim freely but not to drown. The water used was clean and clear, without any additives.

Table 1. Time of passing the Morris water maze before the beginning of the experiment.

Control group (Seconds)	Group № 1 (Seconds)	Group № 2 (Seconds)	Group № 3 (Seconds)
30	27	33	32
32	29	31	28
29	32	30	31
33	31	28	29
28	26	27	32
32	33	32	30
30	28	26	28
34	26	32	27
29	30	30	26
28	29	27	30
26	29	31	27
30	31	29	31
30	33	28	32
29	28	27	33
27	29	31	32
28	30	32	27
29	32	29	28
31	30	30	30
32	31	31	26
27	30	28	29
29,7	29,7	29,6	29,4

Table 2. Melatonin levels before Porsolt's forced swim test.

Control group pg/ml	Group № 1 pg/ml	Group № 2 pg/ml	Group № 3 pg/ml
12,6	14,4	15,1	21,8
16,8	16,6	14,5	12,7
18,7	18,5	20,0	19,6
14,9	17,9	19,6	14,5
14,9	19,1	18,7	15,2
16,6	16,4	17,9	17,5
21,1	19,7	16,5	19,4
19,0	21,1	19,1	14,8
14,6	14,8	17,7	20,9
15,9	15,6	19,8	19,7
18,2	14,9	16,6	17,8
19,2	16,9	15,6	19,9
17,3	17,7	14,7	17,8
16,9	16,6	14,8	15,7
15,1	14,7	15,9	19,6
15,2	15,2	18,6	20,1
17,9	20,1	19,6	15,3
19,6	17,9	22,1	20,1
20,1	18,8	20,8	14,3
19,3	19,1	15,9	19,1
17,195	17,3	17,675	17,79

The aim of the methodology of staging this model-controlling the improvement of cognitive function after chronic stress in the form of forced swimming.

Rats were placed in water on different sides of the maze. A training session was conducted before recording the control results so that the animals could memorise the location of the platform.

Then the rats were given the opportunity to pass the maze without hints. The time for which the rats from 4 groups passed the platform was recorded, as well as the route and behaviour.

After the maze, the study rats were divided into 4 groups of 20 rats each.

The average time to complete the maze before the experiment was calculated:

1. Control group - 29.7 seconds.
2. Group №1 - 29.7 seconds.
3. Group №2 - 29.6 seconds.
4. Group №3 - 29.4 seconds.

The time of passing the maze differs insignificantly.

Table 1 reflects the mean time to complete the Morris water maze prior to the experiment.

In the second step, blood materials were collected from the tail vein of rats of each group to assess melatonin and cortisol levels before the experiment.

Reference values were obtained using STAT FAX 303 analyser (USA). The data were entered into Table №1 (melatonin level) and Table 2 (cortisol level).

Mean melatonin and cortisol values for each group were calculated:

1. Control group - melatonin 17.195 pg/ml, cortisol 32.155 mcg/dl.
2. Group №1 - melatonin 17.3 pg/ml, 33.135 mcg/dl.
3. Group №2 - melatonin 17.675 pg/ml, 31.985 mcg/dl.
4. Group №3 - 1 melatonin 7.79 pg/ml, 30.01 mcg/dl.

Table 2 reflects the melatonin level in each experimental group before stress therapy.

Table 3 shows the cortisol level in each experimental group before stress therapy.

After all preparatory measures, the rats were subjected to the Porsolt forced swimming test.

This test was performed in two stages: at the first stage intact animals were placed for 15 minutes in a transparent Plexiglas cylinder filled with water, the second stage was carried out after 24 hours, where the animals were again placed in a container with water under the same conditions as on the first day. The following parameters were recorded: the latent period of immobilisation, the total time the rat was immobilised, the duration of active swimming, the duration of passive swimming and the number of jumps out of the water. At the end of the set time, the animal was returned to the cage.

As a result of testing, an increase in the time of active swimming and active resistance attempts by 40 % ($p < 0.05$) was found, characterised by an increase in the number of jumps of animals of experimental groups, which indicates a high emotional reactivity of animals.

Following the Porsolt Forced Swim test, rats were reintroduced to the Maurice water maze to assess their cognitive abilities

after stress.

The mean time to complete the maze was calculated:

Average time to complete the maze:

1. Control group - 47.5 seconds.
2. Group № 1 - 38.2 seconds.
3. Group № 2 - 33.5 seconds.
4. Group № 3 - 47.4 seconds.

Table 4 reflects the average time to complete the Morris water maze after the start of stress treatment and drug administration.

After the stress test, blood from the tail vein of the rats was collected again. Cortisol levels increased in all groups including the control group. However, melatonin levels changed to a different degree in each group.

Control group - decreased melatonin levels both individually in each rat and the average level in the group. (Melatonin group average 11.445 pg/ml, decreased by 5.75 pg/ml, cortisol 60.962 mcg/dl, increased by 28.8 mcg/dl).

Group №1 - Melatonin group mean 13.5 pg/ml, decreased by 3.8 pg/ml, cortisol 60.198 mcg/dl, increased by 27 mcg/dl.

Group №2 - Melatonin group mean 17.565 pg/ml, decreased by 0.11 pg/ml, cortisol 57.431 mcg/dl, increased by 25.4 mcg/dl.

Group №3 - Melatonin group mean 11.515 pg/ml, decreased by 6.27 pg/ml, cortisol 55.98 mcg/dl, increased by 25.9 mcg/dl.

Conclusion.

The results show that the control group significantly worsened their performance after stress, increasing the average time to complete the maze from 29.7 to 47.5 seconds. Rats receiving low doses of melatonin also worsened their performance, increasing the time from 29.7 to 38.2 seconds. Rats receiving high doses of melatonin performed the best, with virtually no increase in maze time (increasing time from 29.6 to 33.5 seconds). The group receiving choline alphoscerate showed similar results to the control group, significantly increasing the maze time from 29.4 to 47.4 seconds.

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