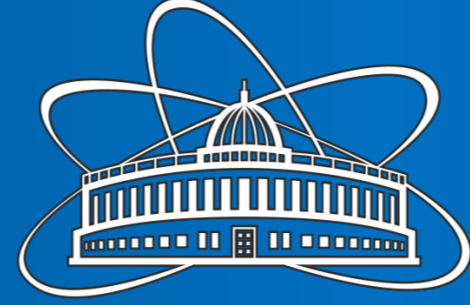


Pharmacological intervention of negative effects of protons with the drug «Cerebrolysin»



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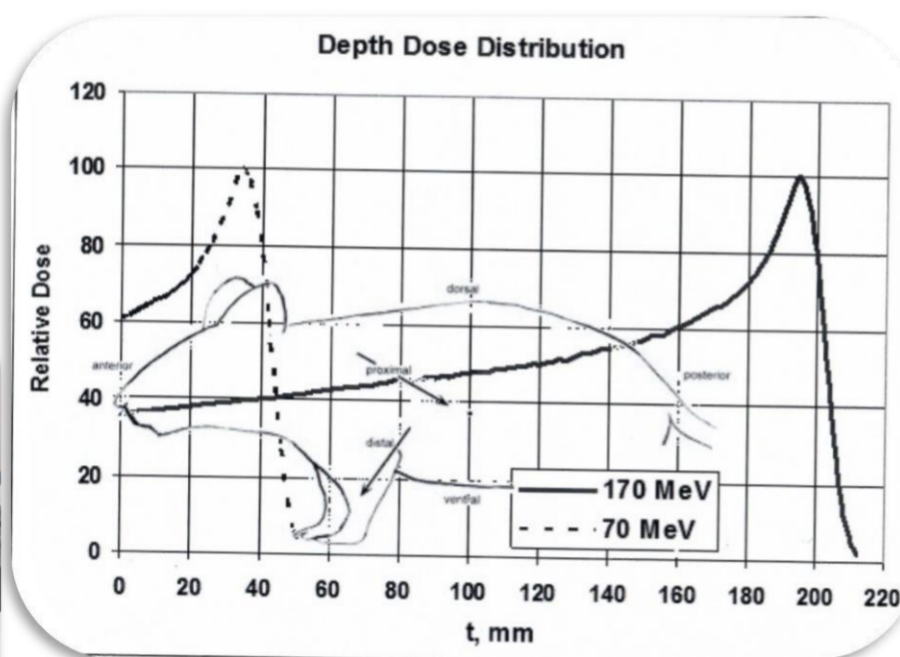
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Introduction

The production of nuclear energy, the use of diagnostic radiation or radiation treatment, or work in radiation-harmful conditions, including research laboratories, can cause human exposure. It is known that radiation exposure can have variety effects on the body, tissues, cells etc. The experiment was conducted to obtain a view of what may occur with behavior of laboratory animals using «Cerebrolysin» after irradiation in the long term.

Material and Methods

- 32 male Sprague-Dawley albino rats weighting 350-360 grams at the age of 4 months at the experiment.
- The animals were irradiated totally with protons, at a dose of 4 Gy, at a rate dose of 0.7 Gy/min, with energy of 170 MeV, at the Phasotron of the Medical and Technical Complex JINR. Three groups were irradiated in the cranio-caudal direction.



Irradiation at the Phasotron of the Medical and Technical Complex JINR

- The laboratory rats were divided into 4 groups ranging in weight: №1 – the group that received intraperitoneal injections of «Cerebrolysin» (2.5 ml/kg); №2 – control group that received injections of NaCl (0.9%, 1 ml); №3 – irradiated group that received intraperitoneal injections of «Cerebrolysin» (2.5 ml/kg); №4 – irradiated group that received injections of NaCl (0.9%, 1 ml).
- Immediately before irradiation, all rats were placed in transparent irradiation containers. The animals of control group were not irradiated, however, they were placed in transparent irradiation containers as well.
- All injections were made on the 32nd day after the irradiation once a day for 2 weeks.



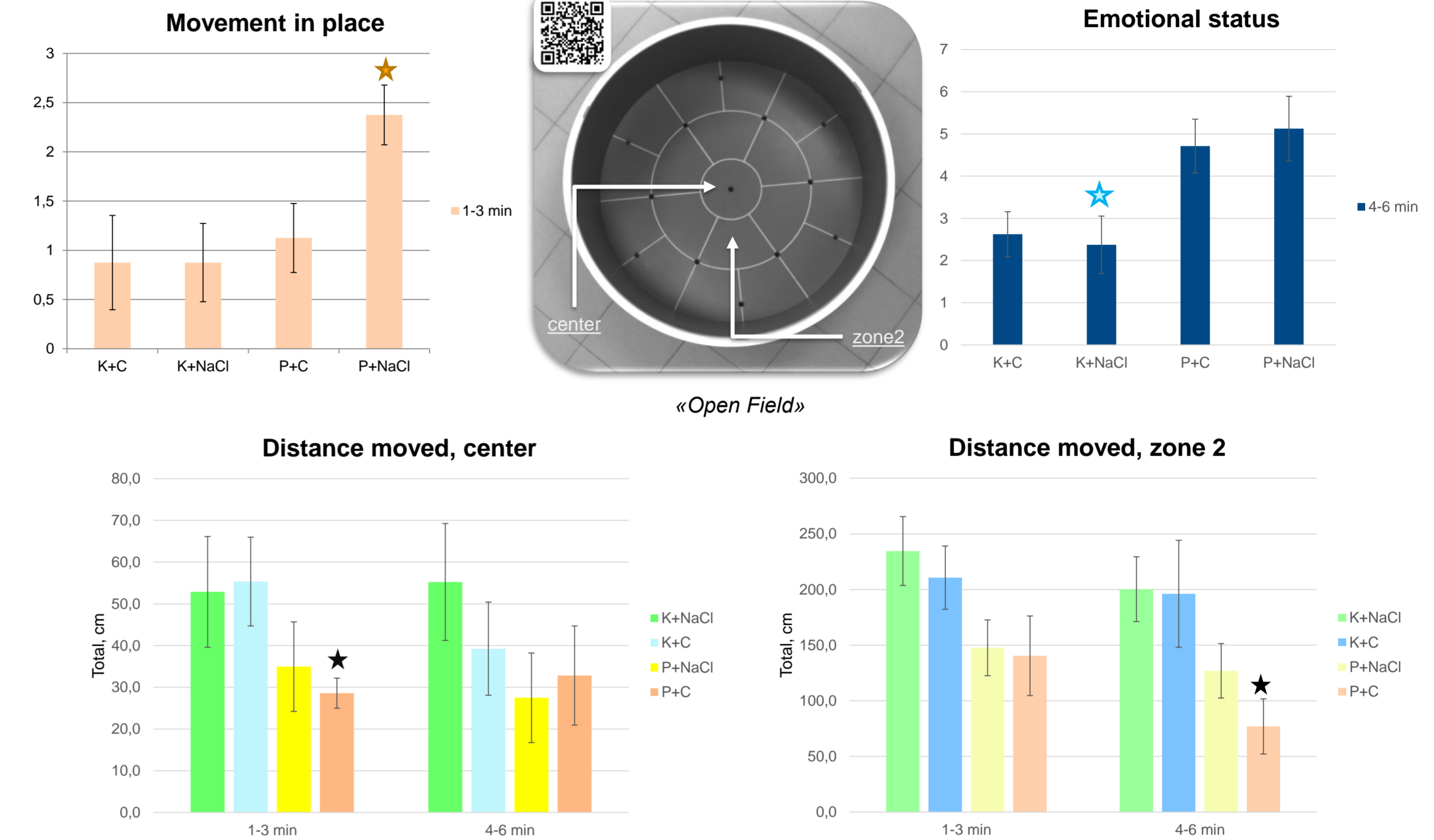
- The behavior of rats was observed and recorded in the Open field test (OF), T-maze and Morris-maze, 50-60 days after the irradiation and injections. The animals were pre-adapted in the treatment room for 30 minutes prior to the testing. The laboratory animals were tested in one maze per day.
- Video recording of animals' behavior was performed using the EthoVision XT 13 software package.

The assessment of the indicators of behavioral reactions of rats was carried out according to the level of locomotor activity in the maze «Open Field» (OF). Automatic analysis was carried out: the total distance moved in the arena, the distance along and close the walls, intermediate and central zone of the maze arena. The following indicators were also manually calculated: the number of sectors crossed, centers, vertical stands up, holes, grooming, freezing, movement in place, defecation/urination. During the experiment, the working memory of rodents was also evaluated during spontaneous alternation in the T-maze. The percentage of alternations, repetitions and rejections was estimated. The spatial memory of rats was evaluated by testing animals in the Morris Water Maze. Next indicators were obtained: 1) the latent release time during which the rat finds the platform and climbs onto it; 2) the path that the animal passes from the place of placement in the water to the platform. For each day, the average value of the latent time, the distance traveled for 3 attempts was calculated.

- Statistical significance was calculated by the Mann-Whitney criterion ($p < 0.05$).
- The experiment was carried out in accordance with the Directive 2010/63/EU of the European Parliament and of the Council of the European Union on the protection of animals used for scientific purposes. In the experiment, the single-blinded approach was used.

Results

1. The analysis of the data revealed a statistically significant increase in the indicator of emotional status and movement on the spot for 50 days in irradiated animals relative to the control group. In irradiated animals receiving the drug, the above indicators were at the control level. With repeated administration of «Cerebrolysin» to irradiated animals, a statistically significant recovery of the "movement in place" indicator (1-3 minutes of testing) to control values was observed. When analyzing the total distance traveled in 1-3 minutes of testing in the OF, it was revealed that in the group of irradiated animals with the introduction of the drug, the value of this indicator was statistically significantly ($p=0.04$) higher than in the irradiated group without the introduction of the drug, which indicates increased motor activity.



2. According to the results of the T-maze, in the group of irradiated animals treated with «Cerebrolysin», a decrease in failures of up to 13% was revealed compared to the irradiated group without drug administration (63%).



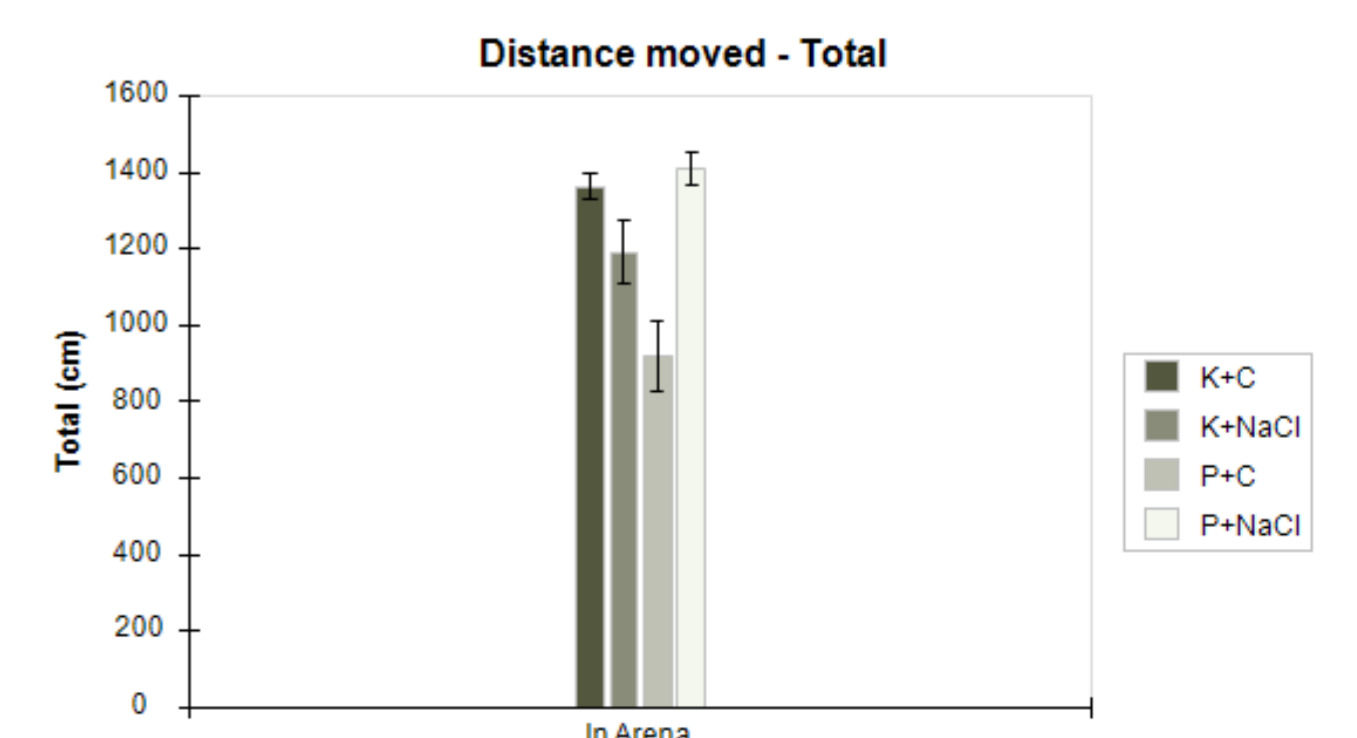
3. There was a statistically significant difference in the distance traveled in the test arena on day 5: the irradiated animals receiving the drug were less active and passed 918.6±91.1 cm compared to the groups №1, 2, 4 (1363.9±35.5; 1191.8±82.7; 1411.4±44.3).

Group/days	1	2	3	4
K+C	43,2±4,2	28,2±4,0	18,7±2,7	17,9±2,5
K+NaCl	43,2±4,5	25,7±4,3	19,8±3,8	14,2±3,1
P+C	44,0±3,7	28,5±4,5	21,2±3,1	17,8±3,6
P+NaCl	36,7±3,8	28,3±4,2	17,2±3,1	15,9±3,3



Morris water maze

Time to reach the platform, sec



Conclusions

Administration of «Cerebrolysin» to irradiated animals statistically significantly restores the value of the indicator «movement in place» (OF) of irradiated animals. According to the results of the T-maze test in the group of irradiated animals receiving the drug, the restoration of spatial working memory of the control group indicators was noted.



Noldus, Wageningen, the Netherlands

The laboratory animal nursery «Pushchino»

