The effect of ionizing radiation on functional activity of the mouse retina

Introduction

The retina consists of terminally differentiated cells that have lost their ability to divide. It is relatively highly resistant to radiation. Nevertheless, we have one retina for all our life and a large contingent of people find themselves in a situation where the level of genotoxic exposure exceeds the level of retinal resistance or the type of influence on the retina is not adaptive: in the radiotherapy of brain, nasopharynx or eye tumors and melanoma. For example, the total dose to the radiotherapy of the nasopharynx and the eye usually ranges from 65-70 Gy. The study of the mechanisms of exposure to various types of ionizing radiation on the retina is fundamental importance for investigating the danger in course of prolonged manned spaceflight. When astronauts are fling to Mars, they will be exposed to different radiation sources - solar and galactic cosmic rays, neutron and gamma radiation. Solar cosmic rays consist mainly of protons of various energies. In this case, the reaction of the retina to the radiation effect may not appear immediately, but in a prolonged period of time after exposure.

It was showed that radiation (accelerated protons) effects are characterized by a non-linear dose–response curve: there is a radioresistance plateau on the graph «dose – effect», indicating that retinal repair mechanisms take place (fig. 1). Noticeable morphological destruction of the retina took place after exposure to accelerated protons at dose more than 14 Gy [1]. Also such doses lead to the changes in the functional activity of the retina.

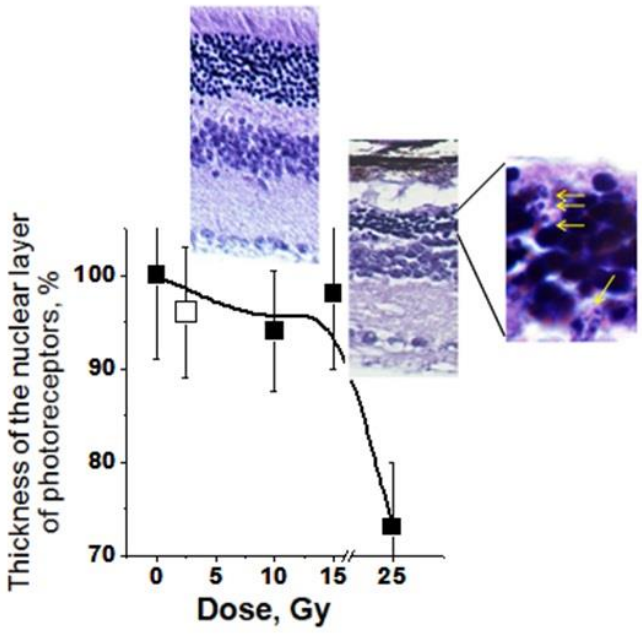


Fig.1. Graph «dose – effect» which is showing morphological changes of the retina after different doses of accelerated protons.

It was showed that an adaptive dose (1 Gy, protons) protects the retina from degeneration induced by chemical agent methylnitrosourea (MNU). The mechanism of protection include suppression of the apoptotic death of photoreceptor cells and decrease induction of DNA double-stand breaks in cells of the retina, compare to MNU in cytotoxic dose (possibly, their repair activation). It has found possible participation of Müller glial cells in retinal cellular damage repair. Müller glia are the principal glial cell in the retina and provide structural and metabolic support to all neuronal cell types. Müller glial cells were stimulated to proliferate in response to a toxic injury and produce bipolar cells and rod photoreceptors. We have showed that the number of Müller cells increases in response to the cytotoxic injection of the chemical agent (fig. 2).

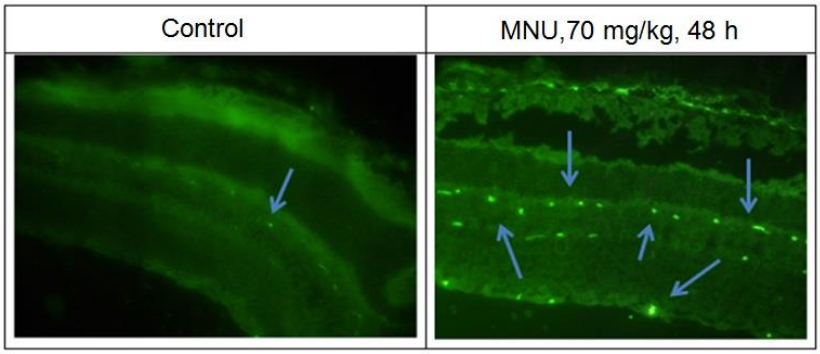


Fig. 2. Micrographs of sections of the retina of mice which are showing activation of Muller cells in the retina after injection of methylnitrosourea in a cytotoxic dose of 70 mg/kg.

The aim of this project is to assess effect of ionizing radiation on functional activity on the mouse retina.

On the basis of the Laboratory of Radiation Biology of JINR we have an opportunity doing researches on the retina with electroretinography.

Electroretinography is an eye test used to detect abnormal function of the retina (the light-detecting portion of the eye) of the anesthetized mice. Specifically, in this test, the light-sensitive cells of the eye, the rods and cones, and their connecting glial Muller cells in the retina are examined. During the test, an electrode is placed on the cornea to measure the electrical responses to light of the cells that sense light in the retina at the back of the eye. The electrodes measure the electrical activity of the retina in response to light. The information that comes from each electrode is transmitted to a monitor where it is displayed as two types of waves, labeled the a-waves and b-waves (fig. 3). This test is useful in evaluating acquired disorders of the retina.

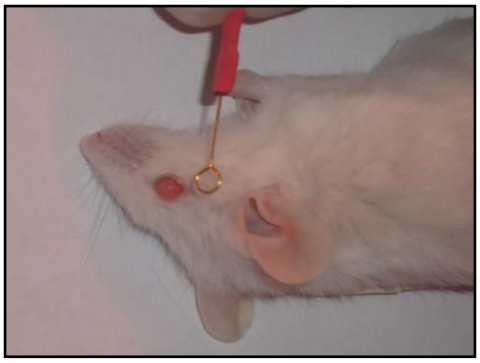
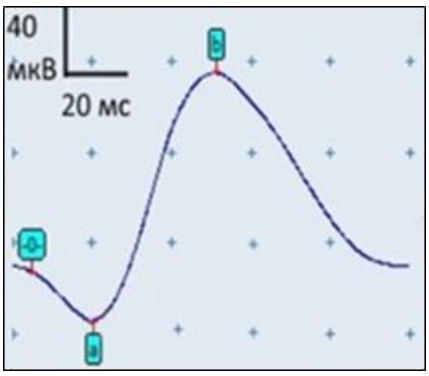
A  B 

Fig. 3. A. the mouse and the eye electrode. B. a-waves and b-waves of electroretinogramm of the mouse.

Student activity:

1. Work on live mice, including its anesthesia and application of electrodes.
2. Irradiation of mice with ^{60}Co γ-rays (the Rokus-M facility) or accelerated protons (the therapeutic beam of the Phasotron).
3. Analysis of the obtained data.
4. Prepare a report.

Number of participants:

This project is meant for 2 students.

Experience:

1. Experience working on animals (or to be ready working on mice careful).
2. Course of Radiobiology will be welcome.

Recommended literature:

1. Gorgels T., Pluijm I., Brandt R. Retinal degeneration and ionizing radiation hypersensitivity in a mouse model for cockayne syndrome. Molecular and Cellular Biology. 2007. V.27. P. 1433–1441.
2. http://webvision.med.utah.edu/book/electrophysiology/the-electroretinogram-clinical-applications/
3. http://www.iar.unicamp.br/lab/luz/ld/Pesquisa/webvision.pdf

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