COMPUTER SIMULATION OF RADIATION-INDUCED DYSFUNCTION OF THE NEURAL NETWORKS OF THE PREFRONTAL CORTEX

A. Bugay [a], ***E. Dushanov*** [a], ***E Popova*** [b*]

[a] *LRB JINR, Dubna, Russia*

[b] *Skolkovo Institute of Science and Technology, Neurobiology and Brain Restoration Center, Moscow, Russia*

The study of the effect of radiation on the brain and its cognitive functions is currently an urgent problem. There are natural sources of radiation and artificial, created by man. Natural radiation is cosmic radiation, the dose of which increases with altitude. For flights at high altitudes, their effect must be considered. Man-made sources of radiation require special precautions, such as measures to control the operation of nuclear power plants, precautions when handling radioactive materials, the inevitable dose of radiation when used in medicine (radiation therapy). The aim of our work is a computer simulation of radiation-induced disruption of the neural networks activity of the prefrontal cortex for various options for doses of radiation. To do this, we used a working memory neural network model, which describes neural activity at various input parameters corresponding to different doses of radiation.

Keywords: Cosmic radiation – Neural activity – Radiation risks

1. INTRODUCTION

Estimation of radiation damage to the central nervous system has become an on-going challenge for the last decades primarily due to the issues of brain tumor radiotherapy [1] and radiation protection for manned flights beyond the Earth's magnetosphere [2–4]. The crew and passengers on high altitude air flights are also facing some degree of cosmic rays radiation.

* E-mail: popovaelp@mail.ru

When assessing the risk of radiation exposure during the prolonged manned flight beyond the magnetosphere it is important to bear in mind the possible formation of disturbances from the central nervous system of pilots and astronauts. In experiments on the irradiation of laboratory animals with high-energy iron ions at doses corresponding to the real fluxes of galactic iron nuclei, when flying to Mars, various disorders from the central nervous system are detected [5]. They are manifested in pronounced disorders of memory, spatial orientation, inhibition of cognitive functions, which is associated with structural and functional changes in brain neurons such as shrinkage in soma size, loss or regression of dendrites and dendritic spines , and disturbance of synaptic transmission and plasticity [6, 7].

In order to have predictive value for risks, biological pathways and their outputs need to be organized into mathematical models. Development of mathematical models for neural networks and structures seems to be an extremely important part in such research. In neuroscience, a biological neural network is a series of interconnected neurons whose activation defines a recognizable linear pathway. The interface through which neurons interact with their neighbors usually consists of several axon terminals connected via synapses to dendrites on other neurons. If the sum of the input signals into one neuron surpasses a certain threshold, the neuron sends an action potential at the axon hillock and transmits this electrical signal along the axon. Biological neural networks have inspired the design of artificial neural networks. Biological neural network simulation have been applied recently for the quantification of related phenomena in hippocampus [8]. This model was used to compare predicted hippocampal CA1 region network firing statistics using input parameters from proton-irradiated versus control mice.

In present work we will study radiation dysfunction of neural activity in the prefrontal cortex that is responsible for short-term retention of information about the object (working memory).

2. MAIN EQUATIONS

Working memory is the ability to transiently hold and manipulate goal-related information to guide forthcoming actions. The prefrontal cortex (PFC) is the brain structure most closely linked to working memory. PFC neurons show elevated persistent activity [9] during delayed reaction tasks, when information derived from a briefly presented cue must be held in memory during a delay period to guide a forthcoming response. The activity is grouped within so called memory fields related to selected object.

For modeling networks which produce persistent firing in response to novel input patterns and thought to be important in working memory and other information storage functions one possible mechanism for maintaining persistent

firing is dendritic voltage bistability in which the depolarized state depends on the voltage dependence of the NMDA conductance at recurrent synapses. Our approach is based on modified version of the model by Sanders et al [10]. The bistability here arises from the complementary nonlinear voltage dependence of GABAB/KIR and NMDA synaptic conductances.

The network is composed of $N_P = 144$ two compartment pyramidal cells (excitatory population) and $N_I = 36$ single compartment interneurons (inhibitory population) according to typical architecture of a cortical module. Hodgkin-Huxley-type conductance-based neurons in the model are connected with each other by spatially structured synaptic contacts with three types of receptors. The excitatory neurons had two compartments: a dendrite with voltage V_d and a soma with voltage V_s. Separating the spike-generating conductances from the bistable synaptic compartment allows bistability to be maintained during the large somatic voltage fluctuations associated with action potential generation.

The equations for the membrane potential of neurons are as follows:

$$C\frac{dU_j}{dt} = -\tilde{g}_L\tilde{z}_L(U_j - \tilde{E}_L) - J_{Na} - J_K - J_{NMDA} \tag{1}$$

$$-J_{AMPA} - J_{GABA_A} - J_{noise}, \tag{2}$$

$$C\frac{dV_{s,i}}{dt} = -g_c(V_{s,i} - V_{d,i}) - g_L z_L(V_{s,i} - E_L) - I_{Na} - I_K - I_{GABA_A}, \tag{3}$$

$$C\frac{dV_{d,i}}{dt} = -g_c(V_{d,i} - V_{s,i}) - g_L z_L(V_{d,i} - E_L) - I_{NMDA} - I_{AMPA} \tag{4}$$

$$-I_{GABA_A} - I_{GABA_B} - I_{noise} + I_{ext}, \tag{5}$$

where $V_{s,i}$, $V_{d,i}$ and U_i are membrane potentials for pyramidal cells and interneurons, respectively, indexes $i = 1...N_P$, $j = 1...N_I$ correspond to cell number, the membrane capacitance is C = 1 nF. Voltages are given in mV, time in ms, conductivity in mS / cm^2.

Ion currents are

$$J_{Na} = \tilde{g}_{Na}\tilde{m}_j^3\tilde{h}_j(U_j - (\tilde{E}_{Na} + \tilde{z}_{Na})), \tag{6}$$

$$J_K = \tilde{g}_K\tilde{n}_j^4(U_j - \tilde{E}_K), \tag{7}$$

$$I_{Na} = g_{Na}m_i^3h_i(V_{s,i} - (E_{Na} + z_{Na})), \tag{8}$$

$$I_K = g_K n_i^4(V_{s,i} - E_K). \tag{9}$$

General view of the kinetic equation for the gate functions of ion channels corresponds to Hodgkin-Huxley approach:

$$\frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m, \tag{10}$$

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n, \tag{11}$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h. \tag{12}$$

For interneurons

$$\alpha_m = -\frac{0.5(U+35)}{\mathrm{e}^{-0.1(U+35)}-1}, \qquad \beta_m = 20\mathrm{e}^{-(U+60)/18}, \tag{13}$$

$$\alpha_h = 0.35\mathrm{e}^{-(U+58)/20}, \qquad \beta_h = \frac{5}{\mathrm{e}^{-0.1(U+28)}+1}, \tag{14}$$

$$\alpha_n = -\frac{0.05(U+34)}{\mathrm{e}^{-0.1(U+34)}-1}, \qquad \beta_n = 0.625\mathrm{e}^{-(U+44)/80}, \tag{15}$$

where $\tilde{g}_L = 0.1$, $\tilde{E}_L = -65$, $\tilde{g}_{Na} = 35$, $\tilde{E}_{Na} = 55$, $\tilde{g}_K = 9$, $\tilde{E}_K = -90$.

For pyramidal neurons

$$\alpha_m = -\frac{0.1(V+32)}{\mathrm{e}^{-0.1(V+32)}-1}, \qquad \beta_m = 4\mathrm{e}^{-(V+57)/18}, \tag{16}$$

$$\alpha_h = 0.07\mathrm{e}^{-(V+48)/20}, \qquad \beta_h = \frac{1}{\mathrm{e}^{-0.1(V+18)}+1}, \tag{17}$$

$$\alpha_n = -\frac{0.01(V+34)}{\mathrm{e}^{-0.1(V+34)}-1}, \qquad \beta_n = 0.125\mathrm{e}^{-(V+44)/80}, \tag{18}$$

$g_L = 0.1$, $E_L = -80$, $g_{Na} = 45$, $E_{Na} = 55$, $g_K = 18$, $E_K = -80$.

First two types of synaptic connections coming from pyramidal cells are excitatory with glutamate as transmitter. Postsynaptic current formed by N-methyl-D-aspartate (NMDA) receptors has nonlinear voltage dependence, which is referred to the magnesium block defined by concentration C_{Mg}.

For interneurons ($k = 1...N_I$)

$$J_{k,NMDA} = \tilde{g}_{NMDA}\tilde{z}_{NMDA}\frac{U_k - E_{NMDA}}{1 + C_{Mg}\exp(-0.08(U_k - E_{NMDA}))} \tag{19}$$

$$\cdot \sum_{i=1, i\neq k}^{N_p} W_{EI}[i,k]s_{i,NMDA}[V_{s,i}(t)]. \tag{20}$$

For pyramidal neurons ($k = 1...N_p$)

$$I_{k,NMDA} = g_{NMDA}z_{NMDA}\frac{V_{d,k} - E_{NMDA}}{1 + C_{Mg}\exp(-0.08(V_{d,k} - E_{NMDA}))} \tag{21}$$

$$\cdot \sum_{i=1, i\neq k}^{N_p} W_{EE}[i,k]s_{i,NMDA}[V_{s,i}(t)]. \tag{22}$$

Another excitatory current formed by a-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors is linear with respect to postsynaptic voltage.

For interneurons ($k = 1...N_I$)

$$J_{k,AMPA} = \tilde{g}_{AMPA}\tilde{z}_{AMPA}(U_k - E_{AMPA}) \sum_{i=1,i\neq k}^{N_p} W_{EI}[i,k]s_{i,AMPA}[V_{s,i}(t)]. \quad (23)$$

For pyramidal neurons ($k = 1...N_p$)

$$I_{k,AMPA} = g_{AMPA}z_{AMPA}(V_{d,k} - E_{AMPA}) \sum_{i=1,i\neq k}^{N_p} W_{EE}[i,k]s_{i,AMPA}[V_{s,i}(t)]. \quad (24)$$

Here $E_{NMDA} = E_{AMPA} = 0$, $C_{Mg} = 0.15$.

Inhibitory synaptic currents formed by gamma-aminobutyric acid (GABA) type-A and type-B receptors are given by the following expressions:

For interneurons ($k = 1...N_I$)

$$J_{k,GABA_A} = \tilde{g}_{GABA_A}(U_k - E_{GABA_A}) \sum_{i=1,i\neq k}^{N_I} W_{II}[i,k]s_{i,GABA_A}[U_i(t)]. \quad (25)$$

For pyramidal neurons ($k = 1...N_p$)

$$I_{k,GABA_A} = g_{GABA_A}(V_{d,k} - E_{GABA_A}) \sum_{i=1,i\neq k}^{N_I} W_{IE}[i,k]s_{i,GABA_A}[U_i(t)], \quad (26)$$

$$I_{k,GABA_B} = g_G ABA_B \left(0.25 + 0.75 \sum_{i=1}^{N_I} \frac{G_i(t)^4 W_{IE}[i,k]}{G_i(t)^4 + K_d}\right) \cdot \frac{V_{d,k} - E_{GABA_B}}{1 + \exp(0.1(V_{d,k} - E_{GABA_B} + 10))}, \quad (27)$$

where $E_{GABA_A} = -70$, $E_{GABA_B} = -90$.

The dynamics of slow type-B $GABA_B$ receptor is controlled through a cascade of chemical interactions. Here

$$\frac{dG_i}{dt} = K_3 R_i - K_4 G_i, \quad (28)$$

$$\frac{dR_i}{dt} = K_1 T_i (1 - R_i) - K_2 R_i, \tag{29}$$

$$\frac{dB_i}{dt} = k_1 T (B_m - B_i) - (k_{-1} + k_{-2}) B_i, \tag{30}$$

$$\frac{dT_i}{dt} = \frac{1}{1 + \exp(-U_i(t)/2)} - k_1 T_i (B_m - B_i) + k_{-1} B - T_i/\tau_D, \tag{31}$$

$K_d = 17.83$, $K_1 = 0.18$, $K_2 = 0.0096$, $K_3 = 0.19$, $K_4 = 0.06$, $k_1 = 30$, $k_{-1} = 0.1$, $k_2 = 0.02$, $B_m = 1$, $\tau_D = 10$.

Presynaptic signal functions s are defined by the following equations:

$$\frac{ds_{j,GABA_A}}{dt} = \frac{Kf_{GABA_A}}{1 + \exp(-U_j(t)/2)}(1 - s_{j,GABA_A}) - Kr_{GABA_A} s_{j,GABA_A}, \tag{32}$$

$Kf_{GABA_A} = 12$, $Kr_{GABA_A} = 0.1$,

$$\frac{ds_{i,AMPA}}{dt} = \frac{Kf_{AMPA}}{1 + \exp(-V_{s,i}(t)/2)}(1 - s_{i,AMPA}) - Kr_{AMPA} s_{i,AMPA}, \tag{33}$$

$Kf_{AMPA} = 12$, $Kr_{AMPA} = 1$,

$$\frac{ds_{i,NMDA}}{dt} = \alpha_s x_i (1 - s_{i,NMDA}) - \beta_s s_{i,NMDA}, \tag{34}$$

$$\frac{dx_i}{dt} = \frac{\alpha_x}{1 + \exp(-V_{s,i}(t)/2)}(1 - x_i) - \beta_x x_i, \tag{35}$$

$\alpha_s = 0.1$, $\beta_s = 0.01$, $\alpha_x = 10$, $\beta_x = 0.5$.

The spatial distribution of network connections is defined through the synaptic weights:

$$W_{EE}[i,k] = \frac{w_{EE}}{\sqrt{2\pi}\sigma_{EE}} \exp\left[-\frac{(\theta_E i - \theta_E k)^2}{2\sigma_{EE}^2}\right], \tag{36}$$

$$W_{EI}[i,k] = \frac{w_{EI}}{\sqrt{2\pi}\sigma_{EI}} \exp\left[-\frac{(\theta_E i - \theta_I k)^2}{2\sigma_{EI}^2}\right], \tag{37}$$

$$W_{II}[i,k] = \frac{w_{II}}{\sqrt{2\pi}\sigma_{II}} \exp\left[-\frac{(\theta_I i - \theta_I k)^2}{2\sigma_{II}^2}\right], \tag{38}$$

$$W_{IE}[i,k] = \frac{w_{IE}}{\sqrt{2\pi}\sigma_{IE}} \exp\left[-\frac{(\theta_I i - \theta_E k)^2}{2\sigma_{IE}^2}\right], \tag{39}$$

where $\theta_E = N_E/360$, $\theta_I = N_I/360$,

The inputs to the network were simulated as follows. The axons representing the pattern to be remembered fired a train of action potentials that was generated by current pulse $I_{ext} = 30$ during the first 100 ms.

Noise was implemented as independent excitatory and inhibitory conductance noise rand drawn at each time step 300 ms from a uniform distribution.

$$J_{k,noise} = g_{noise}(U_k - E_{noise}) \sum_{i \neq k}^{N_i} \widetilde{s}_{i,noise}[\widetilde{V}_{noise,i}(t)], \tag{40}$$

$$I_{k,noise} = g_{noise}(V_{d,k} - E_{noise}) \sum_{i \neq k}^{N_p} \widetilde{s}_{i,noise}[\widetilde{V}_{noise,i}(t)], \tag{41}$$

$$\frac{d\widetilde{s}_{i,noise}}{dt} = \frac{Kf_{noise}}{1 + \exp\Big(-\widetilde{V}_{noise,i}(t)/2\Big)}(1 - \widetilde{s}_{i,noise}) - Kr_{noise}\widetilde{s}_{i,noise}, \tag{42}$$

where $g_{noise} = 10$, $E_{noise} = 0$, $Kf_{noise} = 12$, $Kr_{noise} = 1$.

To simulate random function $\widetilde{V}_{noise}(t)$ the considered time interval is divided into segments of 300 ms and a random moment of time t_0 is generated on them with a normal distribution function over the section being considered

$$\widetilde{V}_{noise}(t) = -80 + 100 \sum_{t_0} \exp\big(-(t - t_0)^2\big). \tag{43}$$

To solve the system, the two program codes were written in MATLAB and C++. Finally the systems of these equations was solved by the Runge-Kutta method. Typical simulation result is shown in Fig.1.

EFFECT OF RADIATION ON THE NEURAL NETWORK OF THE PREFRONTAL CORTEX

At the current level of knowledge it is not possible to develop self-consistent theoretical model of radiation-induced damage to critical sites of neurons. Existing models of charged particle interaction with neurons are only available to count energy deposition events in critical sites of neural cell [11]. Therefore, we will follow the approach introduced in [8], which is based on the usage of experimentally determined change in parameters of neural network. In our case required set of model parameters should be estimated from existing experimental data.

Here we will consider the effect of radiation-induced perturbation of brain neurochemistry. The concentrations of monoamines and their metabolites in different brain areas including the prefrontal cortex were shown to be affected by ionizing radiation [13,14]. It is suggested that the effect of dopamine on working memory

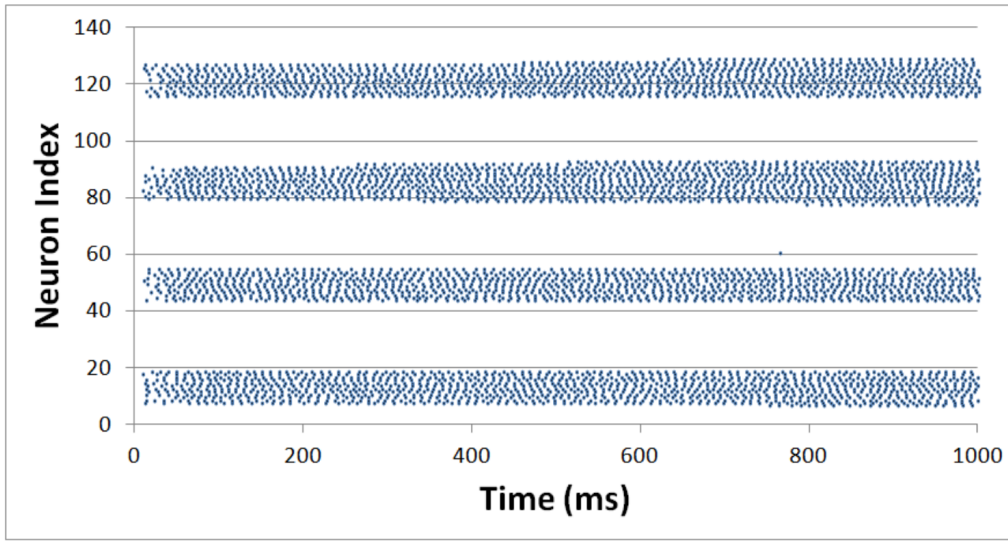


Fig. 1. The activity of neural network (pyramidal cells from 1 to 140 are shown). Four groups of stimulated pyramidal cells (bars correspond to spikes of action potentials) do not spread their activity to other cells. Single neurons in the activated column maintain their firing after external stimulation ends($t = 100$ ms).

performance is mediated by D1 receptors. Dopaminergic modulation via the D1 receptor affects transmission through the AMPA and NMDA receptors, persistent sodium current, and the spontaneous activity of interneurons.

In [12] a similar model was used to simulate the impairment of working memory in schizophrenia. Using a biologically plausible prefrontal cortical circuit model, authors simulated sustained activity during a simultaneous, multitarget working memory task. Hypodopaminergic modulation resulted in imprecision and a reduced capacity in working memory primarily due to decreased NMDA conductance. Increasing NMDA conductance ameliorated both impairments. We can use such model under conditions of radiation exposure.

The modulation of conductivities in our model depends on parameter z, as in [12].

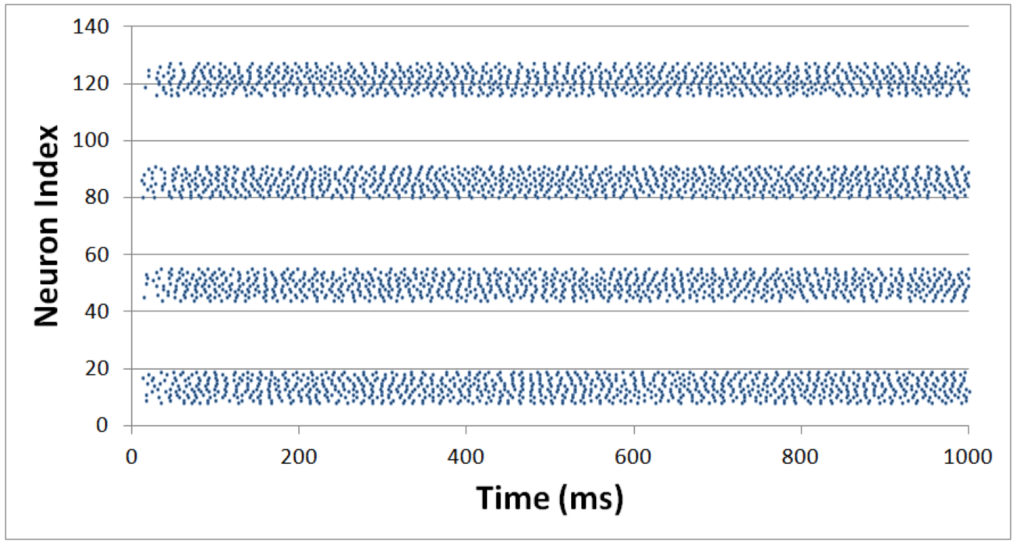
For exitatory neurons:

$$z_{AMPA} = \frac{1.0 + e^{-1.0/0.6}}{1.3 + e^{-1.0/0.6}} \frac{1.3 + e^{(2.0-zda)/0.6}}{1.0 + e^{(2.0-zda)/0.6}},$$

$$z_{NMDA} = 1.88 \frac{1.0 + e^{-1.0/0.6}}{2.0 + e^{-1.0/0.6}} \frac{2.0 + e^{(2.0-zda)/0.6}}{1.0 + e^{(2.0-zda)/0.6}},$$

$$z_{L} = \frac{1.0 + e^{-1.0/0.6}}{0.4 + e^{-1.0/0.6}} \frac{0.4 + e^{(2.0-zda)/0.6}}{1.0 + e^{(2.0-zda)/0.6}},$$

a)



b)

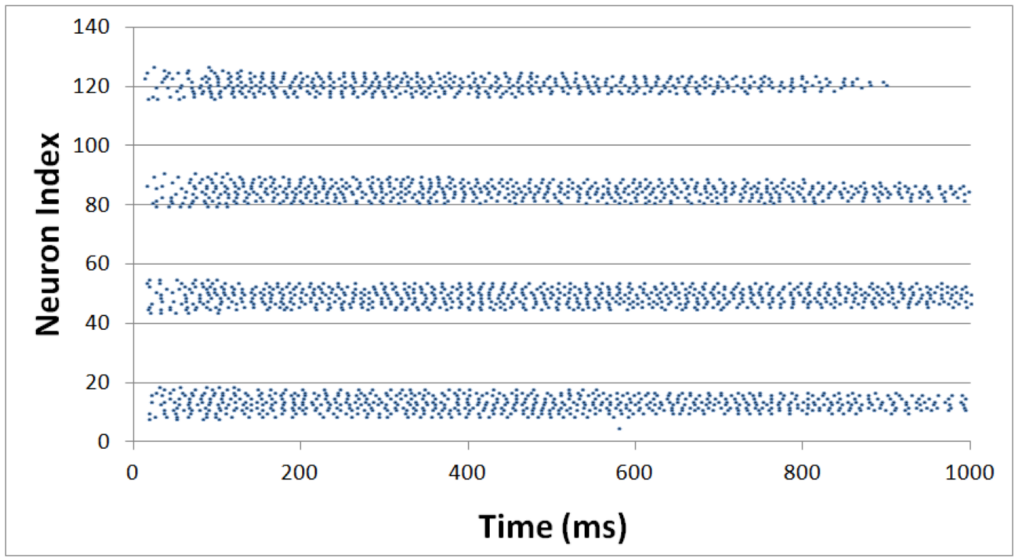
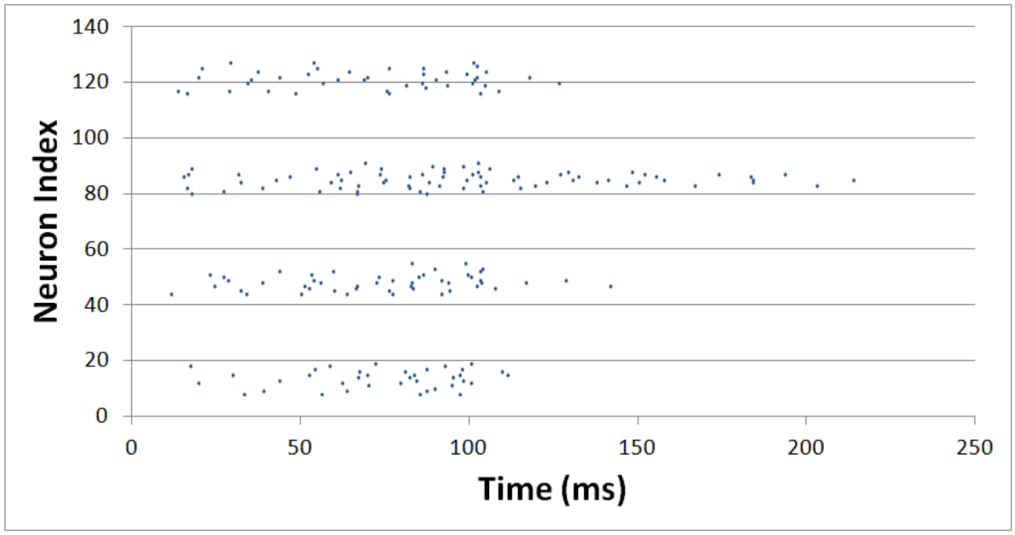


Fig. 2. Simulation of neural network activity after irradiation of 170 MeV protons with doses of 1 Gy (a) and 2 Gy (b) . The initial conditions are the same as in control shown in Fig.1.

$$z_{Na} = 1/(1 + e^{(2-zda)/0.6}) - 1/(1 + e^{(2-3)/0.6}).$$

a)



b)

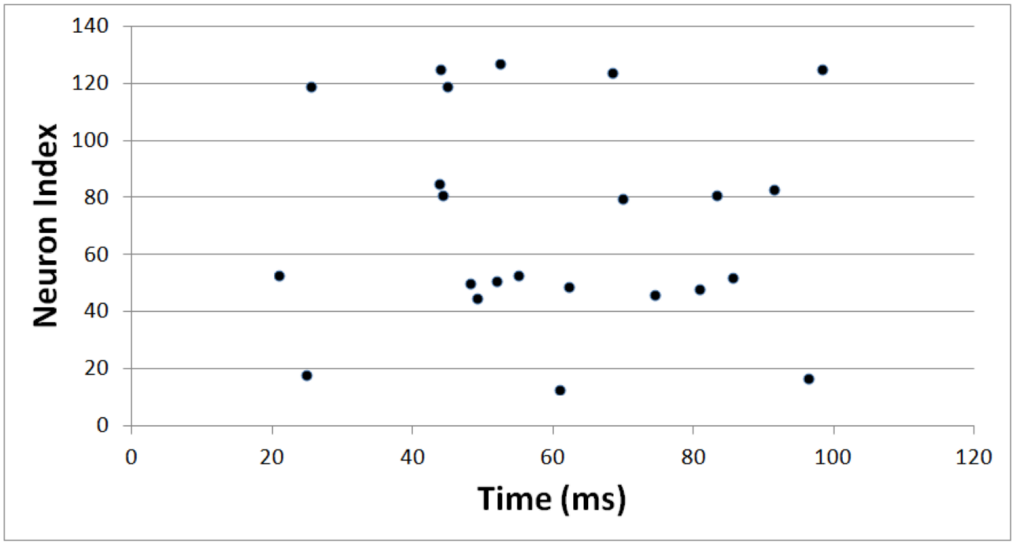


Fig. 3. Simulation of neural network activity after irradiation of 600 MeV/n iron ions with doses of 0.25 Gy (a) and 0.5 Gy (b) . The initial conditions are the same as in control shown in Fig.1. All four groups of stimulated pyramidal cells have lost their ability to maintain firing after external stimulation.

For inhibitory neurons:

$$\tilde{z}_{AMPA} = \frac{1.0 + e^{0.5/0.75}}{1.3 + e^{0.5/0.75}} \frac{1.3 + e^{(3.5 - zda)/0.75}}{1.0 + e^{(3.5 - zda)/0.75}},$$

$$\tilde{z}_{NMDA} = \frac{1.0 + e^{0.5/0.75}}{2.0 + e^{0.5/0.75}} \frac{2.0 + e^{(3.5-zda)/0.75}}{1.0 + e^{(3.5-zda)/0.75}},$$

$$\tilde{z}_{L} = \frac{1.0 + e^{0.5/0.75}}{0.4 + e^{0.5/0.75}} \frac{0.4 + e^{(3.5-zda)/0.75}}{1.0 + e^{(3.5-zda)/0.75}},$$

$$\tilde{z}_{Na} = 1/(1 + e^{(3.5-zda)/0.75}) - 1/(1 + e^{(3.5-3)/0.75}).$$

In normal state $zda = 3$.

In [13] it was shown that irradiation with heavy charged particles leads to more severe cognitive deficits than when exposed to light particles.

For 170 MeV protons (1 and 2 Gy) we have $zda = 2.47$ and $zda = 2.38$ respectively, and for 0.6 GeV/u ^{56}Fe ions (0.25 and 0.5 Gy) $zda = 2.175$ and $zda = 1.65$ according to the experimental data retreived from [13, 14] . The reason for mentioned alterations in not firmly established yet. Along with direct damage to sensitive structures from traversing particle tracks there may be secondary effects such as oxidative stress caused by reactive oxygen species.

In our model simulation with data for 170 MeV protons (1 and 2 Gy) gives weak disturbances in the working memory Fig.1, while irradiation by 0.6 GeV/u ^{56}Fe ions (0.25 and 0.5 Gy) gives a strong deterioration in the working memory Fig.3.

This results correlate with recent experimental findings [15], where uncertainty attending to the possible disruption of cognitive performance caused by proton irradiation was found at the doses of several Gy. The experiments with accelerated iron ions [16] revealed cognitive disorders with doses an order lower than for protons. Such observations support the reliability of our model.

CONCLUSION

We have developed biophysical conductance-based neural network model of working memory for study of radiation-induced impairments. The model can be used to show how known dose-dependent changes in basic parameters of neurons affect network spatiotemporal dynamics. It is demonstrated, that radiation-induced alterations in the properties of synaptic receptors cause loss of stability for specific patterns of activity. This instability arises at very low doses of heavy charged ions, but than for protons.

Proposed theoretical approach provides an insight on how can new knowledge and data from molecular, cellular and tissue models of CNS adverse changes be used to estimate CNS radiation risks.

Acknowledgement This work was supported by Russian Foundation for Basic Research (grant No. 17-29-01007).

REFERENCES

1. Greene-Schloesser D., Robbins M.E., Peiffer A.M., Shaw E.G., Wheeler K.T., Chan M.D. Radiation-induced brain injury: a review // Front Oncol, 2012, V.2, pp.73.

2. Grigoriev A.I., Krasavin E.A., Ostrovsky M.A. The problem of the radiation barrier during piloted interplanetary flights // Her. Russ. Acad. Sci., 2017, V. 87, pp.63.

3. Cucinotta F.A. Review of NASA Approach to Space Radiation Risk Assessments for Mars Exploration // Health Phys., 2015, V. 108, pp.131.

4. Sapetsky A.O., Ushakov I.B., Sapetsky N.V., Shtemberg A.S., Kositsin N.S., Timofeev N.N. Radiation Neurobiology of Long-Term Spaceflights // Biol. Bull. Rev., 2017, V. 7, pp.443.

5. Rabin B.M., Joseph J.A., Hunt W.A., Dalton T.B., Kandasamy S.B., Harris A.H., Ludewigt B. Behavioral endpoints for radiation injury // Adv. Sp. Res., 1994, V. 14, pp.457.

6. Parihar V.K., Allen B., Tran K.K., Macaraeg T.G., Chu E.M., Kwok S.F., Chmielewski N.N., Craver B.M., Baulch J.E., Acharya M.M., Cucinotta F.A., Limoli C.L. What happens to your brain on the way to Mars // Sci. Adv., 2015, V. 1, pp. e1400256.

7. Vlkolinsky R., Titova E., Krucker T., Chi B.B., Staufenbiel M., Nelson G.A., Obenaus A. Exposure to ^{56}Fe-particle radiation accelerates electrophysiological alterations in the hippocampus of APP23 transgenic mice // Radiat. Res., 2010, V. 173, pp.342.

8. Sokolova, I.V., Schneider, C.G., Bezaire, M., Soltesz, I., Vlkolinsky, R., Nelson, G.: Proton radiation alters intrinsic and synaptic properties of CA1 pyramidal neurons of the mouse hippocampus // Radiation Research 2015. V. 183, P.208-218.

9. Goldman-Rakic, P.S.: Cellular basis of working memory // Neuron, 1995, V. 14, pp.477-485.

10. Sanders H., Berends M. , MajorG. , Goldman M. S., Lisman J. E., NMDA and GABAB (KIR) conductances: the "perfect couple" for bistability // Journal of Neuroscience, 2013, V.33. No 2. P.424-429.

11. Batmunkh M., Aksenova S.V., Bayarchimeg L., Bugay A.N., Lkhagva O., Optimized neuron models for estimation of charged particle energy deposition in hippocampus // Physica Medica, 2019, V. 57, pp.88-94.

12. Okimura, T. and Tanaka, S. and Maeda, T. and Kato, M. and Mimura, M.: Simulation of the capacity and precision of working memory in the hypodopaminergic state: relevance to schizophrenia // Neuroscience, 2015, V. 295, pp.80-89.

13. Rabin, B.M., and Joseph, J.A. and Shukitt-Hale, B. and McEwen, J.: Effects of exposure to heavy particles on a behavior mediated by the dopaminergic system // Adv. Space. Res., 2000, V. 25, pp.2065-2074.

14. Shtemberg, A.S. and Kokhan, V.S. and Kudrin, V.S. and Matveeva, M.I and Lebedeva-Georgievskaya, K.D. and Timoshenko, G.N. and Molokanov, A.G. and Krasavin, E.A. and Narkevich, V.B. and Klodt, P.M. and Bazyan, A.S: The Effect of High Energy Protons in the Bragg Peak on the Behavior of Rats and the Exchange of Monoamines in Some Brain Structures // Neurochemical Journal, 2015, V. 9, No. 1, pp. 66-72.

15. Rabin, B.M., and Heroux, N.A. and Shukitt-Hale, B. and Carrihill-Knoll, K.L. and Beck, Z. and Baxter, C.: Lack of reliability in the disruption of cognitive performance following exposure to protons // Radiat Environ. Biophys., 2015, V. 54, No.3, pp.285-295.

16. Britten, R.A. and Davis, L.K. and Jewell, J.S. and Miller, V.D. and Hadley, M.M. and Sanford, L.D. and Machida, M. and Lonart G.: Exposure to Mission Relevant Doses of 1 GeV/Nucleon ^{56}Fe Particles Leads to Impairment of Attentional Set-Shifting Performance in Socially Mature Rats // Radiation Research, 2014, V. 182, pp.292-298.