UDC [УДК] 612.06
DOI 10.17816/transsyst201843s1340-350

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THE MODEL FOR STUDY OF INFLUENCE OF MAGNETIC FIELDS ON BIOLOGICAL OBJECTS (WITHIN THE RUSSIAN MAGLEV PROJECT)

Aim: methodological aspects of the study influenced static magnetic fields (SMF) used in the technology “Russian Maglev” on the organisms are improved.

Materials and methods: organotypic culture of animal tissue fragments was studied under the influence of an experimental setup generating a homogeneous SMF with characteristics similar the “Russian Maglev”.

Results: area index (AI) for liver, heart, prostate, renal tissue of explants in the control and under the action of SMF did not differ. SMF significantly reduces AI of explants the immune tissue of the spleen and the cerebral cortex.

Conclusions: 1. the influence of SMF has a negative impact on the proliferative activity in organotypic culture of the cerebral cortex and spleen; 2. the biological model for examination of influence SMF on organisms intended for approbation of means of physical protection is presented.

Keywords**:** static magnetic field, organotypic tissue culture, “Russian Maglev”, biological model, cell proliferation, means of physical protection.

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МОДЕЛЬ ДЛЯ ИЗУЧЕНИЯ ДЕЙСТВИЯ МАГНИТНЫХ ПОЛЕЙ НА БИОЛОГИЧЕСКИЕ ОБЪЕКТЫ (В РАМКАХ ПРОЕКТА «РОССИЙСКИЙ МАГЛЕВ»)

Цель: совершенствование методологической базы для изучения влияния на организм человека постоянных магнитных полей (ПМП), используемых в технологии «Российский Маглев».

Received: 30.09.2018. Revised: 29.10.2018. Accepted: 17.11.2018.

Материалы и методы: органотипическое культивирование фрагментов тканей животных, на которые воздействовали экспериментальной установкой, генерирующей равномерное ПМП с характеристиками аналогичными отечественной разработке «Российский Маглев».

Результаты: значения индекса площади (ИП) для эксплантатов тканей печени, сердца, простаты, почки в контроле и под действием ПМП не различались. ПМП значительно снижало ИП эксплантатов иммунной ткани селезенки и коры головного мозга.

Выводы:

1. воздействие ПМП отрицательно действует на пролиферативную активность органотипической культуры ткани коры головного мозга и селезенки;

2. представлена биологическая модель оценки влияния ПМП на организмы, предназначенная для апробации средств физической защиты.

Ключевые слова: постоянное магнитное поле, органотипическая культура тканей, «Российский маглев», биологическая модель, пролиферация клеток, средства защиты.

INTRODUCTION

The main attention in the modern scientific literature is paid to operational developments and problems of magnetic levitation transport systems, the energy analysis of the technologies used and developed, the search for optimal technical solutions for safety. The project “Russian Maglev” (RM) is used the system of static magnetic levitation in contrast to electrodynamic (Maglev) and electromagnetic (Transrapid) levitation systems [1]. In this regard, the issues of medical safety of the “RM” have special features, although in the overall structure of the problems they are given insufficient attention. Therefore, it is important to establish the locations and levels of field characteristics around the “RM”, to conduct model medical and biological studies to establish the impact of non-radiation physical fields on various systems of the body, to develop evidence-based proposals and recommendations for the establishment of regulatory norms in this type of transport, to protect against harmful fields effects on passengers and service personnel.

The aim of this work was to study the characteristics of the main sources of static magnetic fields (SMF) used in the technology of “RM” and affecting the human body. The studies in organotypic tissue culture for the differentiated assessment of SMF impact on the organs of different mammalian systems were carried out. It should be noted that the cell and tissue cultures in biological research is increased common as relatively simple model systems is possible to successfully solve many problems the impact of various environmental factors on different organisms.

Organotypic tissue culture is the most appropriate and convenient method for a rapid quantitative assessment by level influenced physical factors on biological

Received: 30.09.2018. Revised: 29.10.2018. Accepted: 17.11.2018.

doi: 10.17816/transsyst201843s1340-350

objects [2, 3]. This is due to the change in the number of cells is the result of stimulation or inhibition of cell proliferation, and this change serves as a criterion for the primary integral assessment of biological activity, including SMF. The advantage of this method is that the explants retain the same hierarchical subordination of the cellular composition of the tissue, as well as in the whole body. In the organotypic culture the strictly dosed effect directly on the cells by SMF is possible to have. This excludes the effect of the whole body nervous, hormonal and other effects. The classical test system is the organotypic culture of various rat tissues.

MATERIALS AND METHODS

The effect of SMF on cell proliferation processes in organotypic tissue culture from different organs mature male rats of the Wistar population ("collection of laboratory mammals of different taxonomic affiliation", Pavlov Institute of Physiology RAS supported by the program of bio-resource collections Federal Agency of Science Organizations from Russia) were studied. The 747 explants of the tissues of the cerebral cortex (n=182), spleen (n=184), kidney (n=95), heart (n=96), prostate (n=92) and liver (n=98) were studied in the experiments. Explants were placed in Petri dishes with a nutrient medium pH=7.2 containing saline (0.9 %) 50 ml, MEM 50 ml, fetal bovine serum 10 ml, glucose (5 %) 1 ml, gentamicin (4 %) 0.5 ml. Petri Dishes with explants were placed in a CO_2 incubator at 36.8°C [4, 5].

The experimental Petri Dishes were exposed in a special camera with a magnetizing device consisting two magnetic poles-concentrators (flat ferrite magnets Y22H ($Fe_2O_3 \cdot SrCO_3$)) with an anisotropic magnetic structure and a platform of non-magnetic material for placing Petri dish with explants of the studied tissue. Concentrators formed a spot of homogeneous SMF, the structure and the amount of induction was controlled by the device Teslameter f 4354/1 at the location studied tissue. The magnitude of the intensity and control of the uniformity of the field in the spot was established and regulated by the mutual location of the concentrators. The measurement error did not exceed 2.5 %. Petri dishes with samples of different tissues was placed between the working ends face of the magnet poles where were within three days at a constant temperature and atmosphere with a homogeneous SMF (~200 mT). The value of the SMF induction value in the experiment corresponds to the SMF intensity in the railway car of the project "RM" at one meter from the floor [6].

The data of two experiments for each tissue included the control Petri dishes without SMF exposure and experimental Petri dishes the with SMF were

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obtained. To quantify the impact of SMF on the development of explants used for morphometric method comparing the control and experimental Petri dishes. For this after the explants were visualized using a microtelevision attachment (series 10, MTN-13, Alpha-Telecom), was calculated area index (AI) using PhotoM 1.2 software.

In the cultivation there is migration cells into the growth zone (GZ) from the Central zone (CZ) of the explant estimated by AI calculating by the formula (1) relationships area (S) the explant (S_{GZ+CZ})) to the area of the central zone (S_{CZ}).

$$AI = \frac{S_{GZ+CZ}}{S_{CZ}} \tag{1}$$

Then, the values of AI were averaged separately for the control AI and experimental dishes AI_E. The Average value of AI_C was taken as 100 %, and the difference of average values (ΔAI) expressed in percent by the formula (2), demonstrates the amount and direction of influence on proliferation of cells.

$$\Delta AI = \frac{AI_E - AI_C}{AI_C} \cdot 100\ \% \tag{2}$$

The reliability of the differences of AI explants in the control and experimental dishes after checking for compliance with the normal distribution of the data was evaluated using t criteria for independent samples. Statistically significant differences were taken at the level of p less than 0.05.

RESULTS AND DISCUSSION

According to previously studied and presented the characteristics of the main sources of SMF in the technology "RM" [6], the magnetic induction exposed to the human body increases from < 1 to 300 mT when approaching the source of MF from 0.7 to 0.1 m, respectively. The data obtained are compared with the current Russian normative and technical documents: SanPiN 2.2.4.3359-16 "Sanitary and epidemiological requirements for physical factors in the workplace" (unfortunately, the regulatory standards in the Russian Federation on transport have not yet been developed). According to the literature data, non-specific reaction by the type of General adaptation syndrome were caused in the human body after exposition of SMF. There is possible specific, similar to the meteotropic, reaction, proceeding with a change in vascular tone. There is a belief that the magnetic factor is not the direct cause of the disease, it only provokes it or contributes to the aggravation of

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Transportation Systems and Technology. 2018;4(3 suppl. 1):340-350
doi: 10.17816/transsyst201843s1340-350

the existing pathological process. People with meteosensitivity may have functional disorders that affect the quality of life. At the same time, the specific dynamics of physiological parameters in different people may be vary [7].

However, the results of screening studies exposure on different organs by SMF the same intensity in the literature could not be found. In addition, only a number of studies have described the study of the characteristics of SMF having the greatest biological effect. There is the most suitable method organotypic tissue culture for the screening study of the action of biologically active factors [8].

According our experimental data uniform SMF with induction of ~200 mT has different effects on the cells of different mammalian tissues. In the Table 1 presents the average values of AI for the explants organotypic tissues culture: liver, heart, prostate, kidneys and we can conclude that proliferative processes are not changed because the values of AI_E statistically not significant different from AI_C. While SMF depressed cell proliferation of immune spleen tissue and brain cells.

Table. The average values of AI for the explants organotypic tissues culture in control (AI_C) and experiment (AI_E)

	cerebral cortex	**spleen**	**liver**	**renal**	**prostate**	**heart**
AI_C, п.и.	1.6±0.26	1.98±0.62	1.67±0.67	2.11±0.78	1.37±0.2	1.79±0.37
AI_E, п.и.	1.29±0.12	1.6±0.34	1.66±0.3	1.76±0.32	1.36±0.2	1.78±0.19
P-value	0.03	0.03	0.83	0.26	0.85	0.65

There is decreasing AI for explants in the experiment compared to the control statistically significantly (P=0.03) for the tissues of the cerebral cortex (ΔPI = –19.7 %) and spleen (ΔPI = –18.9 %).

Despite the above results impact of SMF on living organisms and cells, the long-term practice of SMF application in medical procedures, for example MRI, allowed to publish the works, confirming the safety of SMF application [19, 20]. Although using relatively strong magnetic fields, such procedures can really be safe for patients due to the short duration of magnetic exposure. For the staff, the chronic action of SMF and other harmful factors, allows to neutralize compliance with Sanitary and epidemiological requirements that are non-specific to neutralize the action of SMF [18]. The presented data do not exclude the remote manifestations of SMF by induction 1T exposure for human health [21, 22], although no such effects have been found in other studies [23].

In according to above, there is important to search protection means to reduce the biological effect of SMF on passengers and service men using the transport

Received: 30.09.2018. Revised: 29.10.2018. Accepted: 17.11.2018.
Transportation Systems and Technology. 2018;4(3 suppl. 1):340-350

doi: 10.17816/transsyst201843s1340-350

system "RM". Therefore, in our work we have tried to present the testing model for various neutralization or decrease means of SMF biological effects with the organotypic tissue culture. For this in the 2nd series of experiments, the polypeptides with tissue-specific and stimulating proliferative effect were selected [23, 24] and were introduced into the culture medium for SMF undergone explants. The drug Cortexin® was added to medium of explants the cerebral cortex and Timalin® was added to medium of explants the spleen. These drugs were added at effective concentration 50 nG/ml. Figure 1 shows to decrease statistically not significant the number of AI (ΔAI= –12.3 %) under the action of Cortexin® in explants of the cerebral cortex (thus, the effect of SMF decreased overall by 9 %). The increase of AI statistically not significant was observed in the experimental compared to control the Petry dishes with explants of the spleen undergone combined effect of Thymalin® and SMF (ΔAI =+13.4 %).

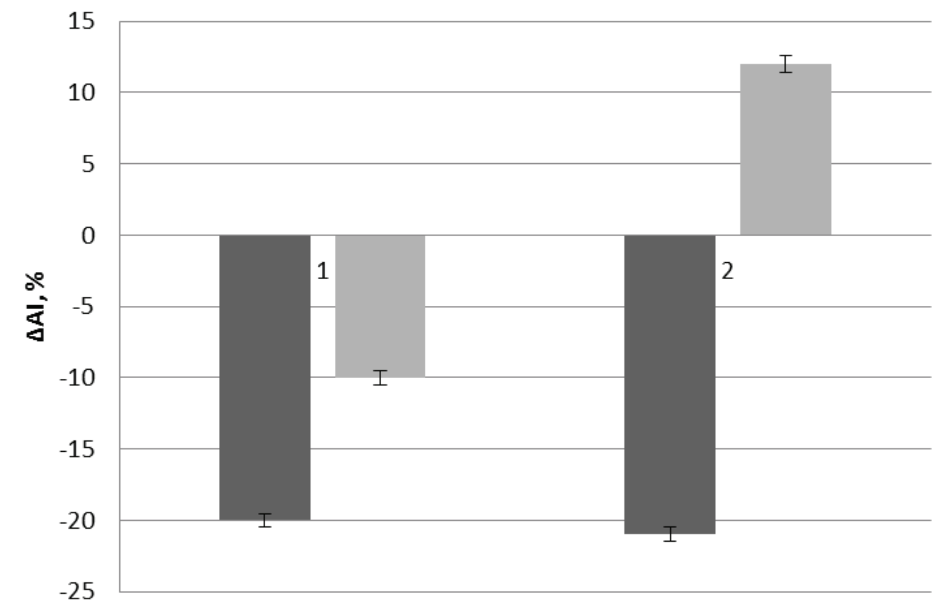

Fig. The SMF influence on the cortex (1) and spleen (2) in isolation (dark bars) and in combination with Cortexin® and Timalin® respectively (light bars)

The data confirm the functional inhibition of proliferative activity explants of spleen and cerebral cortex under the influence of SMF and the normalization proliferative potential under the influence contained growth factors in the used drugs.

Our data have been compared with the other studied data, as the SMF with induction in the range from hundredth to hundreds of mT in the laboratory is created relatively easy. Currently, there is two main areas for scientist's attention of research: the actioned mechanisms of SMF on living organisms are searched and

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Transportation Systems and Technology. 2018;4(3 suppl. 1):340-350
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the biological effects of weak SMF usually with adverse effects on the body are observed. We will discuss the latter direction in more detail. In a number of studies with MF with similar characteristics were obtained cellular effects. In all studies the inhibition of cell proliferation due to an increase in DNA damage when exposed to SMF induction 970 mT [9] or MF with a frequency of 50 Hz and induction 400 mT [10], stimulation of apoptosis MF with a frequency of 50 Hz and induction of 150 mT [11] and SMF with induction 1T [13], increased transcription of genes in SMF with induction 100 mT [15] and damaging effect on the cell membrane with induction of SMF 100–300 mT [17] were described.

However, simple decrease as the induction level of SMF 10–1 000 times then the maximum permissible level (according to 2.2.4.3359-16 “Sanitary and epidemiological requirements to physical factors in working places”) does not neutralize the negative effects of SMF at the cells. According to the literature, enhancing proliferation due to inhibition of apoptosis in SMF with induction of 0.6 mT [12], decreasing the adhesive ability of white blood cells in SMF with induction of 0.05–10 mT [14], increasing the intracellular concentration of heat shock proteins in MF with a frequency of 50 Hz and induction of 10–140 μT [16] are observed. In this regard, there is our direction of research studying the damaging effects of MF with the value of induction and measured characteristics around the “RM”.

CONCLUSION

It was shown, the people need for protection from MF of “RM” system. On the basis of the research listed in this article, the prospect of using the presented biological model in the development and testing of methods and measures to protect against the adverse effects of MF arising from the operation of the magnetic levitation transport system is created. After substantiation of medical and biological safety at the cellular level of technogenic MF system “RM”, it is possible to conduct monitoring studies on real models [26].

The above data allowed us to draw the following conclusions:

1. At the level of the calculated values of the induction of the static magnetic field of the project “Russian Maglev” there is a negative effect on the proliferative activity of the organotypic tissue culture of the cerebral cortex and spleen.

2. The presented biological model of evaluation of the influence of static magnetic fields in the organotypic tissue culture allows to carry out preliminary testing of physical protection means intended for use in the project “Russian Maglev”.

Received: 30.09.2018. Revised: 29.10.2018. Accepted: 17.11.2018.

doi: 10.17816/transsyst201843s1340-350

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Received: 30.09.2018. Revised: 29.10.2018. Accepted: 17.11.2018.
Transportation Systems and Technology. 2018;4(3 suppl. 1):340-350

doi: 10.17816/transsyst201843s1340-350

To cite this article:
Rubinskiy AV, Vlasov TD, Chalisova NI. The Model for Study of Influence of Magnetic Fields on Biological Objects (within the Russian Maglev Project). *Transportation Systems and Technology.* 2018;4(3 suppl. 1):340-350. doi: 10.17816/transsyst201843s1340-350

Цитировать:
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