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BIOCHEMICAL ASPECTS OF THE BIOLOGICAL EFFECT OF A LOW-FREQUENCY PULSED ELECTROMAGNETIC FIELD

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The literature data (Z. V. Gordon, A. S. Presman, Yu. A. Kholodov, etc) indicate a well-expressed biological effect of electromagnetic fields of different frequency ranges.

The biochemical mechanisms on which the morphological and functional disorders arising under the effect of an electromagnetic field are based have been inadequately studied. Meanwhile, such data are extremely necessary if one is to understand the primary mechanisms of interaction of electromagnetic fields with biological objects, to find methods of early diagnosis and develop ways to standardize them.

The task of the present article is to explain the possible biochemical mechanisms of the action of a pulsed low-frequency electromagnetic field on the organism. The selection of precisely that frequency range for study was stipulated, on the one hand, by the increasing use of the energy of a pulsed electromagnetic field with a low frequency (5-50 kHz) in various branches of industry, science, and engineering and, on the other, with a practically complete absence of data on the character of its biological effect. Pulsed electromagnetic fields with an intensity of 24 and 72 kA/m (a frequency of 7 kHz, a pulse length of 130 milliseconds, and an interpulse interval of 10 seconds) were used in conducting the investigations.

The character of the effect of pulsed electromagnetic fields was traced under conditions of multiple effect (15 sessions, daily exposure for 3 hours, and an intensity (I) of 72 kA/m) and chronic effect (1.5, 3 and 6 months, daily exposure for 1.5 hours, and an intensity of 24 kA/m).

The investigations were conducted on 480 male white rats. At the end of the corresponding periods of effect of pulsed electromagnetic fields, and also 1 and 2 months after the chronic irradiation was concluded, in the blood, brain, liver, heart and skeletal muscles determinations were made of a complex of indicators capable of characterizing the state of the carbohydrate-energy and nitrogen metabolism, that is, those types of metabolism which are the basis of the vital activity of the organism. Simultaneously, a study was made of the state of a number of enzymatic processes which permit determining the intimate mechanisms of disorders in those types of metabolism. All the obtained data were processed statistically (M. L. Belen'kiy), in connection with which, in the statement of the factual material, the readings of changes of the studied indicators will relate only to shifts which are reliably determined (at $P \leq 0.05$).

As the investigations showed, the action of a pulsed electromagnetic field causes well-expressed changes in the carbohydrate-energy metabolism of the organism. In all the investigated organs a reduction of the level of macroergic compounds -- adenosine triphosphoric acid (ATP) and creatine phosphate -- is observed. Under the effect of multiple action of a pulsed electromagnetic field (72 kA/m) the level of the latter decreased by 27% on the average in the brain tissue, 45% in the liver, and 30% in the skeletal muscles. Under conditions of chronic effect of a pulsed electromagnetic field (24 kA/m) the reduction of creatine phosphate was 23.8, 55.4 and 26.4% in the brain tissue, 29.3, 59.3 and 40.8% in the heart, and 39.9, 44.9 and 29.2% in the skeletal muscles in the corresponding investigated periods of 1.5, 3 and 6 months. The creatine phosphate content was restored to the level of the control values only after a period of 2 months from conclusion of the action.

In parallel with decrease of creatine phosphate in all those organs, including the liver, there was decrease of the ATP content of the same order of magnitude. Simultaneously, an accumulation of its dephosphorylated derivatives (ADP and AMP) was detected. In the liver the levels of the latter increased by 156 and 120% respectively, in the brain tissue by 20.4 and 66.5%, and in the heart by 57.6 and 36%. Such shifts could occur either as a result of intensification of ATP expenditure in various reactions or when there is disturbance of processes connected with the formation and accumulation of energy in the macroergic bonds of the ATP.

Investigation of the connection of the processes of oxidation with phosphorylation permitted establishing a considerable isolation of those processes in all the investigated organs during both the mutiple and the chronic effect of a pulsed

electromagnetic field. It was greatest in the liver and skeletal muscles, in which the reduction of the R/O ratio was 39.8 and 43.4% respectively, depending on the field intensity and the duration of its effect. In the brain tissue and the heart the degree of isolation of the processes of oxidation and phosphorylation is less considerable, and the isolation itself set in in more remote periods of action of the pulsed electromagnetic field (the third month). Restoration of the connection of those processes in the nerve tissue and heart set in 2 months after the irradiation was halted, whereas in the liver and skeletal muscles the R/O ratio decreased by 11.6 and 13.3% even in that period of the investigation.

Obviously, as a result of isolation of the processes of oxidative phosphorylation there also were shifts in carbohydrate metabolism. In spite of the difference in the degree of connection of the shifts, common to all the investigated organs was a reduction of the glycogen level and a simultaneous accumulation of lactic acid. The most considerable reduction of glycogen was observed in the liver (by 37.4%). In that organ, as in the heart, a very large accumulation of lactic acid also was detected. The level of the latter in those organs in separate periods of the effect exceeded the control values by 60.2 and 68.3% respectively. In parallel with increase of the level of lactic acid in the organs there was also an accumulation of it in the blood.

The obtained results show that under the effect of a pulsed electromagnetic field there is a switching of the decomposition of carbohydrates to a glycolytic path, which can be regarded as a compensatory reaction of the organism under the conditions of isolation of the processes of oxidation and phosphorylation. However, the intensification of glycolysis, which is energetically less effective than the oxidative transformation of carbohydrates, still is unable to compensate the deficit of macroergic compounds forming as a result of isolation of the processes of oxidative phosphorylation.

Disorders of nitrogen metabolism are probably also connected with the shortage of macroergic compounds. As the investigations have shown, the effect of a pulsed electromagnetic field leads to the accumulation of ammonia in the blood, liver, heart, and skeletal muscles and to phase changes of its level in the brain tissue. During multiple effect the ammonia content in those organs increases by 50, 75.3, 25.4 and 39%. In the nerve tissue the ammonia content decreases by 32.6% under those conditions. During chronic effect the directivity of changes in the ammonia level and the degree to which they are expressed are almost the same. The only exception is the nerve tissue,

in which a decrease of ammonia (by 26.2%) was traced in the third month of effect, whereas an increase of its level by 36, 38.3 and 36.3% was observed 1.5, 6 and 1 months after the irradiation was halted. The restoration of the changes in the ammonia level which had been noted in the process of radiation occurred in the heart and skeletal muscles immediately after the irradiation was halted. In the blood and liver those changes were more lasting and were not normalized even 2 months after the action was completed. To clarify the mechanisms of the formation of shifts in ammonia metabolism with consideration of distinctive features of nitrogen metabolism, in each of the investigated organs a study was made of the state of the most important biochemical reactions participating in the formation and removal of ammonia in those organs.

Investigation of the level of glutamine, which is the principal product of the elimination of ammonia at the places of its formation (D. L. Ferdman), permitted detecting a slight increase of it not corresponding to the increase of ammonia, and in individual periods of effect also an absence of changes in the glutamine level. That circumstance, with consideration of data on the absence of changes in the glutaminase activity, shown in vitro for tissues of the brain and liver, indicates a limitation of glutamine synthesis. Investigation of the conditions of the course of glutamine synthesis in homogenates of the brain and liver of animals irradiated by a pulsed electromagnetic field (72 kA/m) permitted establishing that the limitation of that reaction is caused by shortage of ATP which also occurs under conditions in vivo.

Also connected with the shortage of ATP is disruption of the synthesis of urea by the liver, the level of which was reduced by 23.8% under the effect of a pulsed electromagnetic field with an intensity of 72 kA/m and by 17.2% under the chronic effect of a pulsed electromagnetic field with an intensity of 24 kA/m.

Thus on the basis of those investigations it can be concluded that one of the reasons for the accumulation of ammonia in the blood and organs is deceleration of its elimination as a result of an ATP shortage. Side by side with that, study of the state of such processes as the intensity of deamidization of proteins and the deaminization of adenosine and adenylic acid gives grounds for concluding that the accumulation of ammonia is connected not only with deceleration if its elimination in the form of glutamine and urea, but also with intensification of processes of ammonia formation. Determination of the content of amidic nitrogen of proteins, which reflects the state of the processes of their amidization and deamidization, permitted establishing

that the effect of pulsed electromagnetic fields (72 kA/m), without changes its level in the brain and heart, causes a decrease of the latter in the liver and skeletal muscles (by 11.3 and 10.7% respectively). Those data indicate that in the liver and skeletal muscles the amide groups of proteins are one of the most probable sources of increased quantities of ammonia. Simultaneously with intensification of protein deamidization, the action of a pulsed electromagnetic field affects also the intensity of deaminization of adenylic acid. In the brain and liver that process is inhibited, as is indicated by reduction of the adenylate deaminase activity by 17.3 and 11.7% respectively. Those data, besides indicating the participation of that process in the shifts of the ammonia level, also explain the reasons for the accumulation of larger quantities of adenylic acid in those organs. In the heart, ir contrast with the brain and liver, the adenylate deaminase activity is intensified (by 29.7%), and in the skeletal muscles, side by side with activation of the adenylate deaminase (by 21.4%), the effect of pulsed electromagnetic fields intensifies also the adenosine deaminase activity (by 27.2%). Intensification of the deamination of adenosine and adenylic acid undoubtedly is one of the reasons for the accumulation of larger quantities of ammonia in those organs.

Thus the investigations permitted establishing that, in spite of a number of distinctive features relating to concrete mechanisms of the formation of disorders of nitrogen metabolism in individual organs, very characteristic of all the investigated organs (except the brain) is intensification of the processes of ammonia formation, with an absence of corresponding intensification or even inhibition of processes leading to its elimination.

The mechanism triggering those disorders is the isolation of the processes of oxidative phosphorylation, and, as a result of that, disturbance of the supplying of the organism with macroenergetic compounds, which also in most cases is a factor causing disorders of other metabolic units in the organism. Simultaneously with that, the obtained data give grounds for considering that, together with disturbance of the supplying of the organism with macroergic compounds, the reason for shifts developing under the effect of a pulsed electromagnetic field also is disturbances of the activity of a number of enzymatic systems, which lead in the long run not only to functional disorders but also, according to the data of L. N. Yashina et al, to well-expressed morphological changes in the internal organs.

Conclusions. 1. Pulsed low-frequency electromagnetic fields (7 kH) with intensities of 72 and 24 kA/m cause disturbance of carbohydrate-energy and nitrogen metabolism in the brain, liver, heart, and skeletal muscles.

2. The most characteristic shifts in carbohydrate-energy metabolism of all the investigated organs is the formation of a shortage of macroergic compounds (ATP and creatine phosphate), caused by isolation of the processes of oxidative phosphorylation and, as a result of that, intensification of glycolysis (lowering of the glycogen level and accumulation of lactic acid).

3. The action of a pulsed electromagnetic field causes disruption of the transformations of nitrogen compounds, which leads to accumulation of ammonia in the blood, liver, heart, and skeletal muscles and to phase changes of its level in the brain on the background of a slight increase or absence of changes in the glutamine content.

4. Biochemical mechanisms of the formation of shifts in the ammonia level are different and are caused: in the brain -- by inhibition of the deaminization of adenylic acid and deceleration of glutamine synthesis, in the liver -- by inhibition of urea synthesis and intensification of protein deamidization, in the heart -- by intensification of glutamine deamidization and adenylic acid deaminization, and in the skeletal muscles -- by intensification of protein deamidization and the deaminization of adenosine and adenylic acid.

5. On the basis of the degree of expressness of disturbances of carbohydrate-energy and nitrogen metabolism, arising under the effect of a pulsed electromagnetic field, and the periods of their appearance and restoration upon conclusion of the effect, the latter can be arranged in the following order: liver, skeletal muscles, heart, and brain.

6. The presence of a correlation between the disturbance of metabolic processes in the investigated organs and shifts of the biochemical spectrum of the blood permits recommending determination of the content of lactic acid and ammonia in the blood as tests to reveal initial manifestations of the effect of a pulsed electromagnetic field on the organism also under clinical conditions.

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