Interaction of low-level microwave radiation with nervous system – a quasi-thermal effect?

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Abstract. This analytical review is focused on the discussion of a possible interaction mechanism of microwave radiation with the nervous system. Energy level of the non-thermal electromagnetic field effects has a lower boundary, limited by the principal physical noise, and an upper boundary, limited by the thermal effects. The thermal energy that introduces disturbances in energy distribution of ions and movement in neurones is about 10^{-5} eV. The electrical field of 10^{-10} V/cm can introduce an equivalent disturbance of the thermal equilibrium inside a cell of 10 μm radius. If caused by the low-level microwave exposure, this phenomenon may not be associated with an increase in temperature. Fluctuations, initiated by the high-frequency field in the movement of ions and membranes, affect the gating variables and nerve cell properties like the increase in temperature does. The hypothesis that microwave radiation can affect permeability of the membranes of nerve fibres or myelin sheaths was examined experimentally. A 450 MHz microwave field, with and without modulation, polarized perpendicular or parallel to the nerve axon, was applied. The measured field power density at the skin was 0.87 mW/cm^2. The left and right *nervus medianus* motor nerve fibres of two young female subjects were under the study. The results of 20 cycles of measurements show that the low-level microwave field caused statistically significant increase in the nerve pulse propagation velocity in human motor nerve fibre. The increase was detected only for polarization, perpendicular to the nerve fibre. The 100% amplitude modulation decreased this effect. The effect may be related rather to the threshold voltage of the nerve axon than to the myelin sheath.

Key words: EMF effects, low-level radiation, thermal effect, nerve axon, nerve pulse conduction velocity, active membrane permeability.

1. INTRODUCTION

Nervous activity is based on the (bio)electromagnetic phenomena. Signal transmission by the nerve pulse, propagating through the nerve axons and synapses, is a complicated electrical and chemical process. Signal processing and

stimuli analysis in brain need coordinated action of millions of neurones. Since there is a tremendous electrical activity in neural processing and transmission, the nervous system has been thought to be most sensitive to the external electromagnetic field.

Electric and magnetic stimulation of the peripheral nervous system is widely applied in clinical practice for rehabilitation. Transcranial magnetic stimulation (TMS) has become an important tool for brain research and treatment during last decades. In case of electric or magnetic stimulation the low-frequency electromagnetic fields are applied. The frequency of the stimulation is close to physiological frequencies of the system. The interaction mechanisms are not exactly clear yet, but they are obviously based on the effect of the external field on the movement of the ions in neurones and on possible cyclotron magnetic resonance.

Frequency of the microwave radiation is much higher than physiological frequencies. No adequate interaction mechanism of it with the nervous system has been proposed. This is one of the reasons why the thermal effect as the only possible mechanism of interaction has been accepted for microwaves. Absorbed in nervous tissues microwave energy produces heat and the temperature rises if the thermoregulatory mechanisms are not able to suppress heating. Thermal effect occurs at high power levels when specific absorption rate (SAR) is higher than 4 W/kg. Microwave heating (temperature rise about 1 K) is known to affect memory and learning [1–3]. An increase of 1 K in colonic temperature, produced by the radio frequency exposure, causes changes in performance and would almost certainly disrupt ongoing learned behaviour [4,5].

Under conditions of low-level intensity, the thermoregulatory mechanisms act in a normal way and the physiological temperature can be maintained by regulatory mechanism of the living system. The calculated temperature changes do not exceed 0.1–0.5 K for intensities of 0.1–1.0 W/cm^2. Non-thermal effects occur at a low absorbed power level (SAR <1 W/kg). These effects are not related to an apparent release of heat but to the direct microwave field effect.

The worldwide discussion about non-thermal effects of the electromagnetic radiation is still going on [6–8]. Despite extensive research in this field during recent decades, the reports of possible effects are often contradictory and the mechanisms behind the effects are still unclear. The difficulties in independent reproduction of the same experimental results cause doubt in these effects. The recent exhaustive overview of the literature on experimental studies results in a conclusion that "at low levels of exposure biological effects may still occur but thermal mechanisms are not ruled out" [7].

Biomedical Engineering Centre of the TUT has been involved in studies on low-level modulated microwave effects on the human nervous system since 1999. The aim of this analytical review is discussion of possible interaction mechanisms based partly on our experimental data and partly on the results reported by other authors. The boundaries for the energy level of the non-thermal effects, depending on the principal physical noise as the lower limit and on the thermal effects as the higher one, are considered.

2. THERMAL NOISE LIMIT AND THRESHOLD SENSITIVITY

The principal question is: does the energy of the physical phenomena, caused by low-level (non-thermal level) microwave radiation, exceed the energy of thermal fluctuations that occur in the body? The level of thermal noise in case of magnetic stimulation is known to be higher than the magnetic energy and the so-called kT paradox is still not solved for the low-frequency magnetic field effects [9,10].

The thermal noise limit for the electric field has been calculated on the basis of a physical model, in which a cell has been considered as a microwave receiver [11–13]. In the first model [11], the thermal noise component in the membrane potential has been taken into account as the root-mean-square variations in the transmembrane potential due to thermal fluctuations. The integral thermal noise inside the equivalent frequency bandwidth of the cell's membrane has been calculated. For a typical spherical mammalian cell (of 10 μm radius), the magnitude of the minimal detectable electric field is 2×10^{-2} V/cm. The level of thermal noise is determined only by the physical temperature of the cell and does not characterize the fluctuation processes in membrane ionic channels.

The paradox is that, according to experimental data, much smaller fields than the calculated thermal noise limit can be detected. The paradox is resolved if the signal averaging effect is taken into account [14]. The averaging period as well as the frequency bandwidth of the cell as a receiver is determined by the same time constant of the membrane. Therefore the calculation of spectral sensitivity seems to be more convenient and adequate way for the evaluation of the sensitivity of the cell. The reason for that is that the threshold sensitivity of the cell to the external electromagnetic field depends not only on the physical temperature and parameters of the cell membrane, but also on the character of the field. The equivalent frequency band of the cell as a receiver (Δf) is fixed by its time constant (resistance and capacitance of the membrane). The equivalent level of the total noise power is $P = kT\Delta f$, where k is the Boltzmann constant. In case of the narrow band or monochromatic electric fields (low-frequency field) the field power at the receiver P_f does not depend on the frequency band of the receiver. In case of the broad-band electromagnetic fields, the field power at the receiver is $P_f = P_{fs}\Delta f$, where P_{fs} is spectral density of the field power. The first approach has been used in [11].

In case of the microwave radiation, the approach of the broadband fields can be applied. This approach was used in [12,13], where the spectral densities of the electrical noise power from different sources were summarized. Let us suppose that microwave field affects a number of ions passing the channel. This presumption has been approved by experimental data at least for calcium channels; the efflux of ions has been shown to change under microwave exposure [15]. Thus we can consider the ionic channels as sensors of the microwave radiation. The internal noise of the receiver consists of the thermal noise at membrane resistance and current noise caused by ionic current of channels.

Two components of the electrical noise, thermal and shot noises are fundamental and well described by a physical theory. The model for the estimation of the level of electrical noise for a cell, due to thermal fluctuations, is based on the Nyquist formula. The shot noise due to fluctuations of current carriers, moving through the ionic channels without additional fluctuations, is described by the Schottky formula. The calculated values of thermal and shot noise on the membrane of a typical mammalian cell, when an average of 10^4 channels are conducting, are characterized by the same magnitudes. The opening–closing fluctuations of the ionic channels can substantially increase the noise level and add an excess noise. The level of excess noise can be substantially higher than the level of the fundamental physical noise.

The spectral sensitivity of a typical cell as a receiver is about 10^{-8} W/cm^2 Hz. The minimum field to which a cell can respond depends on the dielectric permeability and is about 10^{-6} to 10^{-7} V/cm Hz$^{1/2}$ [13].

It is remarkable that a cellular mechanism for "signal averaging" really exists [14]. If a periodic signal of frequency f is applied for an exposure time τ so that there are $f\tau$ cycles, the signal-to-noise ratio improves by the factor of $(f\tau)^{1/2}$. Let us consider the cell as a natural receiver of radiation. It is easy to see that the physics of this phenomenon is the same as of the technical microwave receiver – collection of the signal energy during the measurement time.

3. HYPOTHESIS: A QUASI-THERMAL EFFECT

The estimated threshold sensitivity of the cell to microwave field is much lower than the absorbed power limit for thermal effects. The power of the bioelectrical physiological processes that must provide a normal living obviously exceeds the level of thermal fluctuations and usually does not cause a rise of the temperature. Does it mean that the low-level microwave effects at the power level between the threshold thermal fluctuations and the thermal effect, accompanied by the temperature rise, can really occur?

Non-thermal exposure of cultures of the human endothelial cells to 900 MHz mobile phone radiation has been reported to activate stress response [16]. Results obtained demonstrate that 1-hour non-thermal exposure of cells changes the phosphorylation status of numerous proteins, among them the heat shock protein hsp27. Changes in the overall pattern of protein phosphorylation suggest that mobile phone radiation activates a variety of cellular signal transduction pathways, among them the hsp27/p38MARK stress response pathway.

The recent results in brain cell damage in mammalian brain and blood-brain-barrier (BBB) permeability confirm that extremely low doses of microwave radiation affect the physiology of the brain [17–19]. A pathological leakage over the BBB was combined with a damage to the neurones [18].

The BBB permeability is determined by the structure of the walls of the blood vessels inside the brain. Widening the slots between the cells of vessel walls causes

an increase in permeability. The possible mechanism of the effect can be the following: the microwave field affects cells (for example causes vibration of the membrane), the distances between the cells increase and permeability changes.

The phenomena of the electron and ion polarization in matter have been thoroughly studied both theoretically and experimentally [20]. As a result we can be sure that the internal field structure inside a biological body can be changed by the external electric field. The field-induced polarization can affect membrane potentials and other bioelectrical parameters and through that affect the bio-electrical processes. The high-frequency microwave field can not cause any regular changes in the movement of ions due to their small absorption cross-section (the wavelength of microwaves is much larger than the dimension of cells) as well as to the inertial properties and viscosity of the liquid medium [21]. However, the high-frequency field can cause fluctuations and vibration of the charged particles and membranes. This phenomenon is similar to the effect caused by Brown motion, initiated by temperature: the mobility of the ions and fluctuations in membrane motions are increasing. Even a small difference in temperature (2 K) causes changes in transfer rate coefficients of the gating variables and Hodgkin–Huxley model needs correction of the rate constants with a factor of 3.48 [22]. An increase about 1 K in temperature has been reported to cause changes in mental ability and performance [1–5]. The thermal energy that introduces disturbances in the distribution of ions and movement in neurones is about 10^{-5} eV. The equivalent energy of the electromagnetic field, disturbing the thermal equilibrium in neurones, can be introduced by the electrical field of 10^{-10} V/cm at a cell of 10 μm radius.

If caused by the low-level microwave exposure, this phenomenon must not be associated with any increase in temperature. Anyway, the fluctuations, initiated by the high-frequency field in the movement of ions and membranes, affect the gating variables and nerve cell properties like the increase in temperature does. The difference between the effects, caused by the temperature and the field, depends only on the orientation of the field: the fluctuations caused by temperature do not have spatial orientation, while the oscillations caused by the field are oriented by the field direction.

4. EXPERIMENT: DEPENDENCE OF THE NERVE PULSE PROPAGATION VELOCITY ON THE POLARIZATION OF THE MICROWAVE FIELD

The experimental study was aimed to evaluate the hypotheses about the quasi-thermal effects. Measurements of the nerve pulse propagation velocity with and without the applied microwave field for different polarizations and modulations were carried out. The presumption was that microwave radiation can affect not only BBB and permeability of blood vessel walls but can cause similar changes in other cells [23]. In this case microwave radiation can affect

the permeability of a nerve axon membrane or the fibre myelin sheath. The changes in fibre membrane permeability and conductance affect propagation velocity of the nerve pulse.

4.1. Methodology

The experiment consisted of 20 cycles of measurements of the nerve pulse propagation velocity. Each cycle included five measurements with different microwave exposure conditions: 1) without the microwave field, 2) with continuous microwave field polarized (electrical vector oriented) perpendicular to the nerve fibre, 3) with continuous microwave field polarized parallel to the nerve fibre, 4) with 7 Hz modulated microwave field polarized perpendicular to the nerve fibre and 5) with 7 Hz modulated microwave field polarized parallel to the nerve fibre. Modulation frequency of 7 Hz was chosen, based on findings that this modulation frequency has an effect on human EEG rhythms [24].

The measurement procedure included two steps. At first the electrical stimulation pulse was applied on the wrist and the nerve pulse (amplitude and shape) was simultaneously recorded at a fixed point of the muscle. Secondly the same electrical stimulation pulse was applied to the elbow and the nerve pulse was simultaneously recorded at the same point. The width of the electrical stimulation pulse was 0.1 ms and the current was selected individually for every subject. These values were constant during all recordings for a subject. The surface electrodes were used for nerve pulse recording. The distance between wrist and elbow electrodes was measured on the arm surface. The time delay was calculated as the time interval between the pulse start points on the curve of the wrist and elbow pulses (Fig. 1). The pulse propagation velocity was calculated as a ratio of the distance to the time delay.

The experiments were carried out with two young (22 and 23 years old) female subjects. The subjects were healthy, without any medical disorders. The subjects were sitting in relaxed position, any physical activity was excluded during the experiment. The left and right *nervus medianus* motor nerve fibres were under the study. The current of electrical stimulation pulse was 53 mA for one and 80 mA for the other subject. Ten cycles of measurements were carried out with one subject. The Schwarzer EMG/EPmyos 2/4 plus System (Germany) was used for stimulation and measurement of the nerve pulse parameters.

The statistical analysis for the calculated pulse propagation velocities was done for the recorded data without microwave field and with perpendicular and parallel polarization of the continuous wave (CW) and modulated fields. The mean values and standard deviation of the data were calculated. The relative changes of the nerve pulse propagation velocity were calculated as $[(v_e - v_0)/v_0]100\%$, where v_0 is the velocity without microwave exposure and v_e is the velocity with exposure. The two-tailed Student t-test was used to evaluate statistical significance of differences between non-exposed and exposed to microwave data. The values of p lower than 0.05 were considered significant.
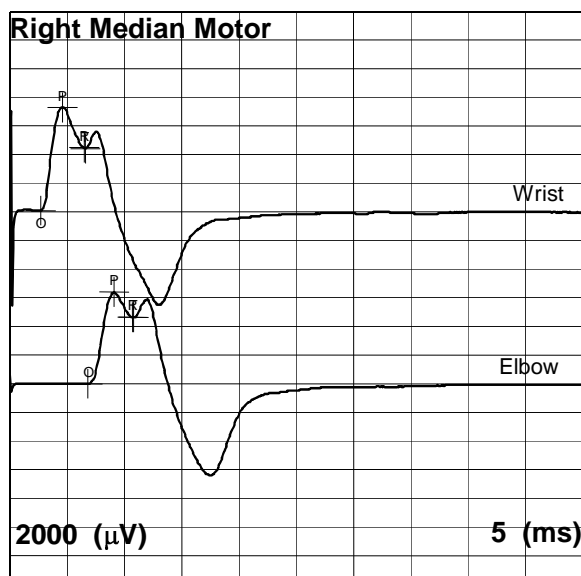
Fig. 1. The experimental protocol for one measurement as printed by the myograph: nerve pulses recorded from the motor nerve fibre *nervus medianus* of the right arm (Right Median Motor); the reference pulse start points are marked as O.

The level of microwave exposure was the same for all recordings. The 450 MHz microwave field was generated by the Rhode & Swarz (Germany) signal generator model SML02. The generator signal was amplified with the Dage Corporation (USA) power amplifier model MSD-2597601. The 1W microwave output power was guided by a coaxial to the 13 cm quarter-wave antenna NMT450 RA3206 by Allgon Mobile Communication AB (Sweden), located at 1 cm from the skin in the middle of the arm. The antenna was placed in two different positions: parallel to the arm and perpendicular to that. During one measurement the microwave radiation was 100% amplitude modulated by the pulse modulator SML-B3 at the frequency of 7Hz (duty cycle 50%).

The Central Physical Laboratory of the Estonian Health Protection Inspection measured the field power density with Fieldmeter C.A 43 of Chauvin Arnoux (France). The microwave field level was monitored during the experiments by the IC Engineering (USA) Digi Field C field strength meter. The measured field power density at the skin was $0.87 \, \text{mW/cm}^2$. The specific absorption rate calculation inside the tissue was based on the measured field power density on the skin. The SAR was calculated as

$$\text{SAR} = \sigma E^2 / 2\rho.$$

For tissue conductivity at 450 MHz, $\sigma = 1.18$ S/m, and density $\rho = 1000 \text{ kg/m}^3$, we obtained SAR = 0.351 W/kg. This formula considers neither the real pattern of field power density distribution inside an inhomogeneous body nor the

reflection from the body surface. The results of numerical calculation, based on the digital anatomical model, taking into account the frequency dependence and possible variations of the dielectric value and conductivity of the tissue [25,26], allowed us to obtain a more reliable estimation of the whole body and localized SAR. In our case (muscle-nerve tissue, 450 MHz frequency), the normalized SAR (W/kg) to EMF power density (mW/cm^2) ratio was 0.06 [26]. Calculations gave SAR = 0.052 W/kg. Thermal effects are extremely unlikely at the levels of the power density used.

4.2. Results

The results of statistical analysis of the measurement data are presented in Table 1. The paired two-tailed Student t-test was applied to detect differences between the values of velocities without and with microwave field in case of different polarizations and modulations.

The data of relative changes of nerve pulse propagation velocity between measurement results without microwave field and with the field perpendicular and parallel to nerve fibre polarization in the cases of continuous wave and modulated field are presented in Fig. 2.

Table 1. The results of nerve pulse propagation velocity measurements

Parameter	Without microwave field	With microwave field			
		CW perpendicular	CW parallel	Modulated perpendicular	Modulated parallel
Average velocity, m/s	57.66	60.06	57.68	58.54	57.72
Standard deviation, m/s	1.58	2.29	1.56	2.33	1.38
p		0.00032	0.69	0.043	0.89
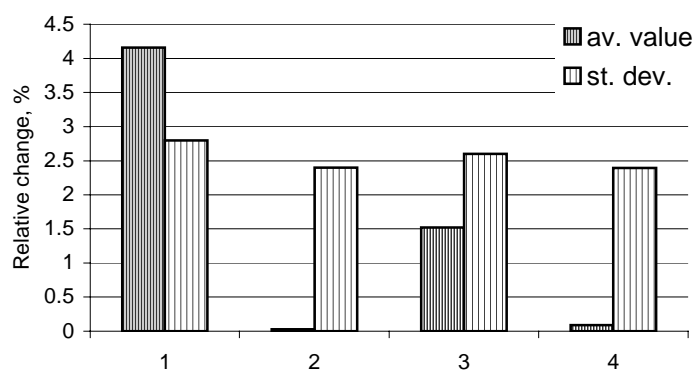
Fig. 2. Relative changes in nerve pulse propagation velocity for different conditions of microwave exposure: 1 – perpendicular polarization of the CW field; 2 – parallel polarization of the CW field; 3 – perpendicular polarization of the modulated field; 4 – parallel polarization of the modulated field.

4.3. Discussion

The measurement data show clearly that the microwave field, polarized perpendicular to the nerve fibre, causes an increase in the nerve pulse propagation velocity and the field polarized parallel to the nerve fibre did not cause any changes in comparison with the normal situation without the field. The obvious dependence of the pulse propagation velocity on polarization also confirms that the effect can not be thermal.

This finding is different from the results of a study on the isolated nerve axon where a short-term exposure to millimetre waves of 1.5 mW/cm^2 did not cause any detectable changes [27]. The effect observed at a higher field intensity (2–3 mW/cm^2) was quantitatively similar to the effect of conventional heating (0.3–0.4 K). In another study it has been reported that microwave pulses alter synaptic transmission by neurone excitation [28]. This result shows that our finding can also be related to the changes in the synapse. The role of synapses was estimated by comparing the recorded time delays when the electrical stimulation pulse was applied on the wrist. This delay was constant during all the measurements for a single person. A possible reason for that may be that the microwave antenna, located in the middle of the arm, causes extremely low level exposure at the synapses area.

The modulated microwave field caused a smaller increase in the nerve pulse propagation velocity than the continuous wave field. The expected effect of modulation, reported in our previous studies on human EEG rhythms and mental ability [24,29,30], does not appear in case of the peripheral nerves. A possible explanation is that the modulation frequency of 7 Hz is related to the mode of the brain waves [31]. Thus in the case of peripheral nerves the modulation is equivalent to the decrease in the radiation power.

The variability of the measurement data is quite high (Table 1, Fig. 2). That may be caused by different factors: uncertainty of the calculation of the time delay, changes in nerve fibre parameters during repetitive stimulation and random error in the location of surface electrodes. The additional increase in the variability of the results was mentioned in the case of applying the perpendicular field. The reason can be different sensitivity of the fibre during different cycles of stimulation and possible random variations in the position of the antenna.

The effect of increasing of the nerve pulse propagation velocity, caused by the perpendicular microwave field, can be related to the changes in the nerve fibre active membrane or its myelin sheath.

The membrane dynamics for nodes of Ranvier in myelinated fibres have been defined in several models [32,33]. The value for nerve pulse propagation velocity in myelinated fibres is valid for the perfectly insulating case of the myelin sheath. Inclusion of the finite impedance myelin caused a reduction of the propagation velocity. An effect of myelin on the conduction was predicted by a theoretical analysis [34,35]. Results for different computer-based cable models of mammalian motor nerve fibres, reported in [36], supported a similar effect. The results were dependent both on the finite impedance characteristic of the

myelin and its model representation. The analysis showed that the propagation velocity was sensitive to the myelin capacitance and to axonal and periaxonal resistivities. These all are parameters that are difficult to measure and for which there are few experimental data.

The microwave field, polarized perpendicularly to the nerve fibre, caused an increase in the pulse wave propagation velocity. While the microwave field caused a decrease in the impedance of the myelinated sheath, the effect predicted by theory is the opposite. Did the microwave field increase the myelin impedance? There is no physical reason for that. The reduction of permeability of the myelinated sheath would be opposite to the trend of changes in BBB [17–19]. There-fore we can suppose that the dependence of the velocity of the nerve pulse propagation on the microwave field is related to the changes in the active membrane of the fibre in the nodes of Ranvier.

The Hodgkin–Huxley model is the most important theoretical model describing the excitable membranes [22]. This model describes the form, amplitude and velocity of the propagating nerve pulse. The conductances for sodium, potassium and chloride ions G_{Na}, G_K and G_L characterize the transmembrane current according to this model. The transfer rate coefficients for different ionic channels depend on the membrane voltage. An important physical property of the membrane is the change in sodium conductance due to activation. The higher value achieved by the sodium conductance results in higher gradient of the voltage, increased local currents, faster excitation and increased conduction velocity. The velocity of the propagating nerve impulse in unmyelinated axon [37]

$$v = \sqrt{\frac{i_{Na}}{r_i c_m^2 V_{th}}},$$

where i_{Na} is sodium current per unit length, V_{th} is threshold voltage, r_i is axial resistance per unit length and c_m is the membrane capacitance per unit length.

The increase in velocity values, caused by the microwave field, may be related to the increase in sodium current, decrease of threshold voltage or reduction of axial resistance. The last parameter is difficult to measure and there are only few experimental data on that. The ions transfer coefficients as well as the threshold of the membrane voltage depend on the temperature and can be affected by the disturbance of the thermal equilibrium caused by the microwave field. Therefore the effect noticed can be rather related to the decrease in the threshold of the membrane voltage.

5. CONCLUSIONS

Energy level of the non-thermal effects has a lower boundary, determined by the principal physical noise, and an upper boundary, limited by thermal effects. The thermal energy that introduces disturbances in ions distribution and movement in neurones is about 10^{-5} eV. The electrical field of 10^{-10} V/cm can

introduce an equivalent disturbance of the thermal equilibrium inside a cell of 10 μm radius without an increase of the temperature. Fluctuations, initiated by the high-frequency field in ions movement and membranes, affect the gating variables and nerve cell properties like an increase in the temperature does. The changes, evoked by the low-level microwave field, can be quantitatively similar to the effect of conventional heating. The quasi-thermal effect is not related to the increase of temperature.

The difference between the temperature- and field-caused effects depends only on the orientation of the field: the fluctuations caused by temperature do not have spatial orientation, but the oscillations caused by the field are oriented by the field. Therefore dependence of the nerve pulse propagation velocity on polarization of the applied microwave field was examined experimentally. The results of the experimental study show that low-level microwave radiation caused relatively small (about 4%) statistically significant increase in the nerve pulse propagation velocity in human arm motor nerves. It is important to point out that the effect depends on the polarization of the applied microwave field: the changes were detected only for the perpendicular to the nerve fibre polarization. These findings support the hypotheses about the quasi-thermal effect.

The mechanism and details of the effect need further investigation.

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Madala nivooga mikrolainekiirguse koosmõju närvisüsteemiga – kas kvaasisoojuslik mõju?

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Analüütilises ülevaates hinnatakse mikrolainekiirguse ja närvisüsteemi võimalikke koosmõjumehhanisme. Elektromagnetkiirguse mittesoojusliku mõju piirang on altpoolt määratud füüsikalise müraga ja ülaltpoolt soojusliku mõjuga. Soojuslik energia, mis tekitab häiritust ioonide energeetilises jaotuses ja liikumises neuronites, on suurusjärgus 10^{-5} eV. Seega elektriväli tugevusega 10^{-10} V/cm on võimeline tekitama ühesuguse häirituse soojuslikus tasakaalus rakkudes raadiusega 10 μm. Madala nivooga mikrolaine kiirguse poolt tekitatud häiritus ei ole seotud temperatuuri tõusuga. Kõrgsagedusliku välja poolt esile kutsutud fluktuatsioonid ioonide liikumises ja membraanides mõjutavad membraanide läbitavust ja raku omadusi sarnaselt temperatuuri mõjule. Eksperimentaalselt uuriti hüpoteesi, et mikrolaine kiirgus mõjutab närvikiu omadusi ja nende kaudu närviimpulsi levi kiirust. Kasutati pidevat ja moduleeritud kiirgust sagedusega 450 MHz, polariseeritud kas risti või piki närvikiudu. Välja võimsustihedus naha pinnal oli 0,87 mW/cm^2. Uuriti motoorset närvi kahe noore naise vasakul ja paremal käel. Kahekümne mõõtetsükli tulemused näitasid, et närvikiule risti polariseeritud väli tingis statistiliselt olulise närviimpulsi levi kiiruse suurenemise. See tulemus kinnitab hüpoteesi mikrolainekiirguse kvaasisoojuslikust mõjust.