

Electromagnetic Fields and Neurodegenerative Diseases

Abstract. The aim of this work is to present the current knowledge about the possible participation of electromagnetic fields in the occurrence and also in treatment of neurodegenerative diseases. The literature data indicate both the negative and positive effects of electromagnetic fields and not allow to draw unambiguous conclusions. Undoubtedly, the topic is still open and needs further intensive research to finally assess the mechanism of action of the electromagnetic field on neurodegenerative diseases.

Streszczenie. Celem niniejszej pracy jest przedstawienie aktualnej wiedzy o możliwym udziale pól elektromagnetycznych w występowaniu oraz w leczeniu chorób neurodegeneracyjnych. Dane literaturowe wskazują zarówno na negatywny, jak i pozytywny wpływ pól elektromagnetycznych i nie pozwalają na wyciągnięcie jednoznacznych wniosków. Niewątpliwie temat jest nadal otwarty i wymaga dalszych intensywnych badań, aby ostatecznie ocenić mechanizm działania pola elektromagnetycznego na choroby neurodegeneracyjne. (**Pola elektromagnetyczne i choroby neurodegeneracyjne**)

Keywords: electromagnetic fields, nervous system, neurodegenerative diseases, transcranial magnetic stimulation (TMS).

Słowa kluczowe: pola elektromagnetyczne, układ nerwowy, choroby neurodegeneracyjne, przezczaszkowa stymulacja mózgu (TMS).

Introduction

The increasing number of artificial sources of electromagnetic fields (EMFs) raises concern about its impact on human health. Beside many beneficial and therapeutic applications of EMFs [1], there are more and more publications describing the unfavourable effect of the EMFs exposure on humans and mostly pointing on the deterioration of well-being, disruption of the nervous system functions or the cancer occurrence. Recently, there have also appeared articles indicating the relationship between the higher incidence of neurodegenerative diseases and the increased exposure to EMFs [2]–[4]. However, the published results are not unequivocal and often contradictory. Researchers try to define a mechanism that could explain the impact of EMFs exposure on the increased incidence of neurodegenerative diseases, suggesting the participation of, among others, oxidative stress. Nevertheless, further research is needed to thoroughly explain the mechanism of action of the EM field on the central nervous system and to explain the potential relationship with neurodegenerative diseases. In this paper, neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) will be briefly presented. Next, the relationship between the incidence of neurodegenerative diseases and the EMFs exposure will be discussed. Also an examples of usage of EM fields in the treatment of neurodegenerative diseases will be described at the end.

A brief description of neurodegenerative diseases

Neurodegeneration is the progressive loss of structure or function of neurons, including death of neurons. There are several hundred neurodegenerative diseases (NDD), and the main difficulty in their classification lies in the fact that their symptoms may coincide with each other. An additional issue in the classification of neurodegenerative diseases is the fact that in many neurodegenerative diseases several areas of the brain are affected (e.g. in multi-system loss) which lead to unspecific clinical picture, moreover different combinations of brain changes may give different clinical symptoms. In addition, the neurodegenerative process itself can affect different areas of the brain at the beginning, giving symptoms that differ from those typical for a given disease. Despite these difficulties, the most common categorization of neurodegenerative disorders is based on: the main clinical features or the topography of the prevailing changes, often both are taken into account [5].

Alzheimer's disease

Alzheimer's disease (AD) is a syndrome of neurodegenerative disorders leading to dementia. The AD brain is characterized by the presence of 2 classes of abnormal structures, extracellular amyloid plaques and intraneuronal neurofibrillary tangles (NFT). The soluble building blocks of these structures are amyloid- β ($A\beta$) peptides for plaques and tau proteins for tangles. Amyloid- β peptides are proteolytic fragments of the transmembrane amyloid precursor protein, whereas tau protein is a brain-specific, axon-enriched microtubule-associated protein [6]. It has been proven that $A\beta$ stimulates the process of apoptosis, or programmed cell death [7, 8]. The behavioural symptoms of AD correlate with the accumulation of plaques and tangles, whose a direct consequences are damage and destruction of synapses that mediate memory and cognition. Synapse loss can be caused by the failure of live neurons to maintain functional axons and dendrites or by neuron death [6]. Senile plaques have a negative effect on neurons and damage them as a result of unexplained mechanisms, it is suspected that they disturb ion balance in nerve cells which results in damage to the nerve signal conduction and altered calcium channel activity in synapses. In turn, the intraneuronal presence of the NFT primarily reduces axonal flow and slows down the metabolism of the neuron to ultimately lead to cell death [7]. In Alzheimer's disease there is a significant decrease in the concentration of acetylcholine, an important neuro-transmitter that participates in memory processes, and also a decrease in the concentration of serotonin, noradrenaline and dopamine.

Scientists don't yet fully understand what causes AD in most people. The molecular basis of Alzheimer's disease is associated with mutations in three genes (15% of cases) in early-onset Alzheimer's disease. Late-onset Alzheimer's arises from a complex series of brain changes that occur over decades. The causes probably include a combination of genetic, environmental, and lifestyle factors as: 1) age, which is one of the most important factors in Alzheimer's disease; 2) sex; 3) low level of education or lack of education; 4) serious head injury or repeated minor injuries; 5) myocardial ischemia; 6) advanced maternal age, increases the probability of occurrence of Alzheimer's disease in a child, and 7) stressors. The association of AD with immune disorders is also suspected. In the etiology of Alzheimer's disease, it is more and more often indicated on the part of oxidative stress, which leads to disturbances of the prooxidative and antioxidative balance [9].

Multiple sclerosis

Multiple sclerosis (MS) is a condition that affects the central nervous system (the brain and the spinal cord) in a variety of ways. Scientists don't know what causes MS but they do know that it provokes an "auto-immune reaction". In this 'auto-immune attack' the body fails to recognise its own tissue (in this case, myelin tissue) as part of itself and the immune system swings into action to destroy it. In MS, the myelin sheath becomes inflamed. Sometimes the inflammation dies down, but if it continues, the myelin is damaged and a scar forms. Scientists have called these scars 'plaques' or 'sclerosis' (from the Greek word for scar). This process is called demyelination (FS-MS). Demyelination causes slowing or loss of nerve conduction [10, 11]. Multiple sclerosis can cause damage in any structure of the central nervous system, which is the reason why the course of the disease is very diverse in each person and depends on the location of demyelinating lesions [11]. The onset of the disease may not be noticeable, and the symptoms of the disease may be transient and mild. Initial symptoms include: 1) sensory disorder on the limbs or face; 2) paresis of a pyramidal limb; 3) impaired motor coordination; 4) total or partial failure to see 5) double vision episodes; 6) impairment; 7) instability of gait; 8) disturbance of balance. One of the most common disorders in the case of MS is visual disturbances. The spectrum of symptoms is very wide and can affect almost every part of our body, which significantly worsens the quality of patient's life [12].

Parkinson's disease

Parkinson's disease (PD) is a progressive neurodegenerative movement disorder associated with the loss of cells in various parts of the brain, including a region called the substantia nigra—one of the main producer of dopamine in human brain. Loss of dopamine causes neurons to fire without normal control, leaving patients less able to direct or control their movement. The exact cause of Parkinson's disease is unknown, although research points to a combination of genetic and environmental factors. The single biggest risk factor for Parkinson's disease is advancing age. Men have a somewhat higher risk than women. The primary symptoms of Parkinson's disease are all related to voluntary and involuntary motor function and usually start on one side of the body. Other symptoms can include: 1) Cognitive impairment; 2) Mood disorders; 3) Sleep difficulties; 4) Loss of sense of smell, called hyposmia; 5) Constipation, speech and swallowing problems [13]. Increasing evidence suggests that oxidative stress is responsible for cell loss in the substantia nigra [14, 15]. The substantia nigra of PD patients exhibit increased levels of oxidized lipids [16], proteins and DNA [17] and decreased levels of reduced glutathione (GSH) [18].

Amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a group of rare neurological diseases that mainly involve the nerve cells (neurons) responsible for controlling voluntary muscle movement. ALS is caused by gradual deterioration (degeneration) and death of motor neurons which initiate and provide vital communication links between the brain and the voluntary muscles [19]. Messages from motor neurons in the brain (called upper motor neurons) are transmitted to motor neurons in the spinal cord and to motor nuclei of brain (called lower motor neurons) and from the spinal cord and motor nuclei of brain to a particular muscle or muscles. In ALS, both the upper motor neurons and the lower motor neurons degenerate or die, and stop sending messages to the muscles. Unable to function, the muscles gradually weaken, start to twitch (it is called fasciculation), and waste

away (atrophy). Eventually, the brain loses its ability to initiate and control voluntary movements [20].

Early symptoms of ALS usually include muscle weakness or stiffness. Gradually all muscles under voluntary control are affected, and individuals lose their strength and the ability to speak, eat, move, and even breathe.

In searching for the cause of ALS, researchers are also studying the impact of environmental factors. The number of possible causes is investigated such as exposure to toxic or infectious agents, viruses, physical trauma, diet, and behavioural and occupational factors.

One of the suggested mechanisms is oxidative stress, which increases the permeability of the mitochondrial membrane and the release of calcium ions. This in turn leads to the death of the cell, and thus the motor neurons of the brain, trunk and spinal cord cortex [19].

Electromagnetic field and neurodegenerative diseases

Researchers are looking for external factors that are responsible for developing the neurodegenerative diseases. Several recent reports indicate that exposure to electric and magnetic fields may be associated with increased risk of NDD, and the most importance is attached to occupational exposure. It has been strengthened in the last decade, for example in the following studies [21]–[25].

Based on an analysis of the death certificates, it was found that among people professionally exposed to electromagnetic fields (e.g. power plant operators) there is higher ratio of death because of neurodegenerative diseases than in other professional groups [26]. However, occurrence of Alzheimer's disease and amyotrophic lateral sclerosis was stronger associated with electric and magnetic field exposition than Parkinson's disease. In similar study [27] the higher mortality rate because of Alzheimer's disease in men exposed to magnetic field is found, but in contrast to the study [26] myotrophic lateral sclerosis deaths was not associated with magnetic field exposure. The increase risk of Alzheimer's disease was also confirmed in an extensive meta-analysis [22]. Study [28] seems to confirm evidence of a relationship between occupational EMF exposure and AD, in which an increased incidence of Alzheimer's disease in males before the age of 75 exposed to EM fields at work, was concluded. Researchers also provided analysis of death rate of people lived in neighbourhood of the high-voltage line. Authors observed increased mortality due to neurodegenerative diseases in particular Alzheimer's disease in residents living nearby (50 m or less) 220–380 kV power lines [3].

In contrary, study [29] in huge analysis based on 30,631 persons does not observed correlation between Alzheimer's diseases and occupational exposure to electromagnetic fields.

In most available data the association between Parkinson disease and electromagnetic field exposure is not observed [22, 29, 30]. However, in [22] the authors found an increased incidence of PD as a result of electromagnetic fields exposure.

Although the publications on the subject of association of EM field and neurodegenerative diseases are quite numerous, it is important to note that all those analysis are based on death certificates and medical documentation only. Many external factors can be important in determining the risk of NDD in different professional groups, such as the severity of work, physical or mental work, and lifestyle. People subjected to occupational exposition of EMF are predominantly physical worker. What is more, the data from death certificates mostly concerns people who lived and worked in the '70, '80 and '90. Such a data may lead to conclusions that are inadequate to the present days.

In *in vivo* and *in vitro* studies conducted in [3] it was shown that EM fields can cause mild oxidative stress (increase in ROS (reactive oxygen species) and changes in antioxidant levels) and is involved in anti-inflammatory processes (reduction of proinflammatory cytokines and increase in anti-inflammatory cytokines). The increase in the level of pro-inflammatory cytokines after exposure to EMF (1–7 mT, and 50 Hz) was also demonstrated in experiments on rats [31].

The participation of inflammatory processes may lead to the activation of microglia and the intensification of oxidative stress caused by the explosion of electrons. Inflammation in the central nervous system often occurs in the case of Alzheimer's disease, Parkinson's disease or in the case of chronic neurological disorders. The cascade of inflammation is initiated by microglia and astrocytes of the central nervous system. The fact that microglia are active in the aging brain and the occurrence of natural neuronal death indicates that the interaction between neuron and glial cells play a significant role in controlling the inflammatory response of the central nervous system [32, 33]. As it was already mentioned, EM field exposure can lead to oxidative stress in the body. In the review [34], author indicates, that the exposure to EMFs (50 Hz, 0.1–1.0 mT) can cause redox reactions and the induction of oxidative stress in the mouse brain. This increases the level of free radicals, which leads to oxidative damage to the lipids in the brain of mice and rats. In the experimental model of the rat, which was exposed to the 50 Hz EM field (100 and 500 μ T), there was a strong toxic effect disturbing the antioxidant effect. It was shown that exposure to 50 Hz frequency electromagnetic field (0.1–1.0 mT), affects the antioxidant capacity of enzymes in both the brain of young and old rats. However, in older rats, a large decrease in all major anti-oxidative enzymes was observed, thus indicating an age-dependent greater susceptibility to induction of oxidative stress as a result of exposure to the EM field [34].

Electromagnetic fields in the treatment of neurodegenerative diseases

Despite the negative influence of electromagnetic fields on the CNS, its positive effects is noticeable and is used in the therapy of many neurodegenerative diseases as shown in the following studies [35]–[37].

Magnetotherapy

Magnetotherapy involves the use of a magnetic field with a magnetic flux density value from 0.1 to 20 mT, and a frequencies up to 100 Hz. Its action on the nervous system consists in improving the metabolism of nerve cells, blood supply to the brain, intensification of synaptic reorganization processes or analgesic effects, in patients with MS receiving magnetotherapy, reduction in muscle tremor, nystagmus, pain, dizziness and better urination control is observed. It was also proved that after magnetotherapy treatment, the functions of damaged cranial nerves were restored. In the case of MS, retrobulbar optic neuritis is common, and after magnetotherapy, visual acuity was improved [38]–[40]. It is worth noting that researchers still design novel applicators for magnetotherapy and their performance is tested both by computer simulation and experiments [41]–[43]. An important problem is also human exposure to electromagnetic fields near various magneto-therapeutic devices [44].

Magnetostimulation

Magnetostimulation is a procedure in which a magnetic field is used (the magnetic flux density values are from 1 pT

to 100 μ T and the basic frequency course ranges from a few to 3000 Hz). Basic waveforms are modulated in such a way that their envelopes have a waveform with frequencies from a few to 100 Hz. The therapeutic cycle should include 14 daily treatments. In selected cases, it is advisable to repeat the cycle after 4 weeks [40, 45]. Magnetostimulation affects the limbic system and the cerebral cortex. Particular indications for magnetostimulation are depression, fatigue syndrome, cognitive disorders and circadian rhythms. Magnetostimulation reduces the symptoms of depression, improves the mood of patients, reduce anxiety. The results of clinical trials confirmed the high therapeutic efficacy of magneto-stimulation using weak variable magnetic fields in the treatment of neurotic symptoms in the course of multiple sclerosis, Parkinson's disease and Alzheimer's disease [46]–[49]. In the paper [50], the authors described positive effects of treatment with EMFs of a patient with chronic progressive MS. Regularly weekly transcortical treatments with pulsed EMFs (4.2 Hz, and 7.5 pT) improved mental functions, returned the strength in the upper extremities, and recovered a trunk control. With prolonged treatment the return of more hip functions and recovery of motor functions in legs were observed. Also about 80% of functions in the upper limbs and hands was regained.

Transcranial magnetic stimulation (TMS)

In the 1980's, researchers introduced TMS into medical practice as a diagnostic tool in neurology for exploring brain function, and for treating neurological disorders such as multiple sclerosis, Parkinson's disease, Alzheimer's disease, autism, Asperger's disorder, substance addictions, neuropathic pain, and schizophrenia [50].

This form of stimulation involves the use of a magnetic field of 2 T and a very short pulse duration (100–200 μ s) with a frequency from 1 to 100 Hz to induce an electric field in the brain [51, 52]. Therapeutic potential lies in repetitive stimulation modulating cortical excitability which also has behavioural consequences. TMS uses EM induction to electrically influence nearby cells. Strong effects can depolarize neurons and trigger action potentials. Low intensity TMS mostly stimulate low-threshold inhibitory interneurons, whereas higher intensities excite axons of neurons [53, 54]. This method allows to stimulate the brain areas located up to 2 cm from its surface [40, 50]. Moreover, an induced electric field might cause several changes in metabolism, neurotransmitters release, and induction of gene expression [47]. TMS holds great potential as a tool for understanding how the brain works, correcting its dysfunctions and even augmenting its abilities [37].

TMS replaced the painful transcranial electrical stimulation, due to the deeper penetration of the magnetic pulse through resistant electrical tissues, this method ensures painlessness and non-invasiveness. The use of TMS to assess the functional status of the central motor neuron enabled a better understanding of the neurophysiological basis of Parkinson's disease. In patients with PD, attempts were made to use rTMS (repetitive TMS – magnetic stimulation with a series of pulses), at a frequency of 0.2, 1 to 5 Hz, which resulted in improved motor function in these patients. In patients with MS, the use of TMS resulted in lowering the amplitude of reflexes and muscle contraction in the lower limb, scientists explain this fact with plastic lesions in the spinal cord under the influence of TMS. Recent studies have indicated that high frequency repetitive TMS has significant therapeutic effect on cognitive function in patients with mild to moderate Alzheimer's diseases [55]–[57]. What is interesting, the TMS issue is successfully analysed in numerous computer studies [58]–[60].

Summary

The aim of this work was to present current knowledge about the participation electromagnetic fields in the occurrence and treatment of neurodegenerative diseases. Neurodegenerative diseases are the increasingly common problem of today's society. This is due to the fact that every year the number of cases of these diseases increase. Currently, in the era of rapid technical progress, people are increasingly surrounded by devices emitting an EM field. Researchers are trying to link these two issues. The thesis that the EM field increases the risk of neurodegenerative diseases generates much lack of clarity.

In the case of Parkinson's disease and multiple sclerosis, there is not enough research to determine whether EMFs affects the development of these diseases. However, some scientists cast a shadow of uncertainty claiming that the electromagnetic field contributes to the formation of oxidative stress in the body and in this way to the occurrence of these diseases. However, in the case of Alzheimer's disease and amyotrophic lateral sclerosis, there are many studies indicating the participation of the EMF in the development of these diseases. Although many results are not consistent, there is an increased risk of AD developing in men, but it is not found in women. The uncertainties in the results of research probably result from insufficient methodology, they are based mainly on death certificates.

It can be assumed that EMFs affects the occurrence of neurodegenerative diseases indirectly, EMFs causes oxidative stress in the body and is involved in the anti-inflammatory process, and these processes may contribute to the development of neurodegenerative diseases. The lack of a sufficient number of tests and literature data does not allow to draw unambiguous conclusions regarding the influence of the electromagnetic field on neurodegenerative diseases.

As it was briefly described above EMFs could be a useful also as therapy for any brain disorder involving dysfunctional behaviour in a neural circuit. EMFs have been tried to employ as a treatment for disorder, schizophrenia, Parkinson's, dystonia (involuntary muscle contractions), chronic pain and epilepsy.

For most of these cases, only a few inconclusive studies currently exist. Nevertheless, interest remains high among researchers who continue of using safe magnetic fields to turn specific brain regions on and off [36]. Undoubtedly, further intensive research is needed to finally assess the mechanism of action of the electromagnetic field on neurodegenerative diseases.

Acknowledgments

The authors would like to thank Donovan Kelorii (LSBA, CELTA) for constructive criticism and copy editing of the manuscript.

Authors: dr Joanna Wyszowska, Nicolaus Copernicus University, Faculty of Biology and Environmental Protection, Department of Biophysics ul. Lwowska 1, 87-100 Toruń, E-mail: joanna.wyszowska@umk.pl;

mgr Milena Jankowska, Nicolaus Copernicus University, Faculty of Biology and Environmental Protection, Department of Biophysics, E-mail: milena.jankowska@umk.pl;
dr inż. Piotr Gas, AGH University of Science and Technology, Department of Electrical and Power Engineering, al. Adama Mickiewicza 30, 30-059 Kraków, E-mail: piotr.gas@agh.edu.pl.

REFERENCES

[1] Gas P., Essential Facts on the History of Hyperthermia and their Connections with Electromedicine, *Przegląd Elektrotechniczny*, 87 (2011), No. 12b, 37-40.

[2] Ahlbom A., Neurodegenerative diseases, suicide and depressive symptoms in relation to EMF, *Bioelectromagnetics*, 22 (2001), No. S5, S132-S143.

[3] Mattsson M.-O., Simko M., Is there a relation between extremely low frequency magnetic field exposure, inflammation and neurodegenerative diseases? A review of in vivo and in vitro experimental evidence, *Toxicology*, 301 (2012), No. 1, 1-12.

[4] Terzi M., Ozberk B., Deniz O.G., Kaplan S., The role of electromagnetic fields in neurological disorders, *Journal of Chemical Neuroanatomy*, 75 (2016), Part B, 77-84.

[5] Przedborski S., Vila M., Jackson-Lewis V., Series Introduction: Neurodegeneration: What is it and where are we?, *The Journal of Clinical Investigation*, 111 (2003), No. 1, 3-10.

[6] Bloom G.S., Amyloid- β and tau: the trigger and bullet in Alzheimer disease pathogenesis, *JAMA Neurology*, 71 (2014), No. 4, 505-508.

[7] Dickson D.W., Apoptotic mechanisms in Alzheimer neurofibrillary degeneration: cause or effect?, *The Journal of Clinical Investigation*, 114 (2004), No. 1, 23-27.

[8] Murphy M.P., LeVine H., Alzheimer's Disease and the β -Amyloid Peptide, *Journal of Alzheimer's Disease*, 19 (2001), No. 1, 311-323.

[9] *Alzheimer's Disease Fact Sheet*, National Institute on Aging. <https://www.nia.nih.gov/health/alzheimers-disease-fact-sheet>

[10] Coggan J.S., et al., Physiological Dynamics in Demyelinating Diseases: Unraveling Complex Relationships through Computer Modeling, *International Journal of Molecular Sciences*, 16 (2015), No. 9, 21215-21236.

[11] Popescu B.F.G., Pirko I., Lucchinetti C.F., Pathology of Multiple Sclerosis: Where Do We Stand?, *Continuum: Lifelong Learning in Neurology*, 19 (2013), No. 4, 901-921.

[12] Murray T.J., Diagnosis and treatment of multiple sclerosis, *BMJ*, 332 (2006), No. 7540, 525-527.

[13] Heyn S.N., Davis Ch.P., *Parkinson's Disease Early and Later Symptoms, 5 Stages, and Prognosis*, Available online at: https://www.medicinenet.com/parkinsons_disease/article.htm

[14] Hirsch E.C., Does Oxidative Stress Participate in Nerve Cell Death in Parkinson's Disease, *European Neurology*, 33 (1993), Suppl. 1, 52-59.

[15] Hwang O., Role of Oxidative Stress in Parkinson's Disease, *Experimental Neurobiology*, 22 (2013), No. 1, 11-17.

[16] Bosco D.A., et al., Corrigendum: Elevated levels of oxidized cholesterol metabolites in Lewy body disease brains accelerate α -synuclein fibrilization, *Nature Chemical Biology*, 2 (2006), No. 5, 249-253.

[17] Nakabeppu Y., et al., Oxidative damage in nucleic acids and Parkinson's disease, *Journal of Neuroscience Research*, 85 (2007), No. 5, 919-934.

[18] Zeevalk G.D., et al., Glutathione and Parkinson's disease: is this the elephant in the room?, *Biomedicine & Pharmacotherapy*, 62 (2008), No. 4, 236-249.

[19] Parsons Ch.G., Danysz W., Amyotrophic lateral sclerosis (ALS), *Therapeutic potential of ionotropic glutamate receptor antagonists and modulators*, (2002), 540-562.

[20] *Amyotrophic Lateral Sclerosis (ALS) Fact Sheet*, National Institute of Neurological Disorders and Stroke. Available at: <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet>

[21] Garcia A.M., Sisternas A., Hoyos S.P., Occupational exposure to extremely low frequency electric and magnetic fields and Alzheimer disease: a meta-analysis, *International Journal of Epidemiology*, 37 (2008), No. 2, 329-340.

[22] Hug K., Rösli M., Rapp R., Magnetic field exposure and neurodegenerative diseases—recent epidemiological studies, *Sozial- und Präventivmedizin*, vol. 51 (2006), No. 4, 210-220.

[23] Lagorio S., Polichetti A., Is ELF-EMF exposure a risk factor for cancer and neurodegenerative diseases? [Online:] http://www.icemb.org/bologna/epidemiologia/EP2_ELF%20over view_ICEmB%202012_final_11%2018.pdf

[24] Santibanez M., Bolumar F., Garcia A.M., Occupational Risk Factors In Alzheimers Disease: A Review Assessing Quality of Published Epidemiological Studies, *Occupational and Environmental Medicine*, 2007. DOI:10.1136/oem.2006.028209

[25] Zhou H., et al., Association between extremely low-frequency electromagnetic fields occupations and amyotrophic

- lateral sclerosis: a meta-analysis, *PLoS One*, 7 (2012), No. 11, Art. No. e48354. DOI: 10.1371/journal.pone.0048354
- [26] Savitz D.A., Loomis D.P., Tse Ch.K.J. Electrical Occupations and Neurodegenerative Disease: Analysis of U.S. Mortality Data," *Archives of Environmental Health: An International Journal*, 53 (1998), No. 1, 71-74.
- [27] Feychting M., et al., Occupational magnetic field exposure and neurodegenerative disease, *Epidemiology*, 14 (2003), No. 4, 413-419.
- [28] Andel, R., et al., Work-related exposure to extremely low-frequency magnetic fields and dementia: results from the population-based study of dementia in Swedish twins, *J. Gerontol. Ser. Biomed. Sci. Med. Sci.*, 65 (2010), No. 11, 1220-1227.
- [29] Johansen C., Exposure to electromagnetic fields and risk of central nervous system disease in utility workers, *Epidemiology*, (2000) 539-543.
- [30] Savitz D.A., Checkoway H., Loomis D.P., Magnetic field exposure and neurodegenerative disease mortality among electric utility workers, *Epidemiol. Camb. Mass*, 9 (1998), No. 4, 398-404.
- [31] Wyszowska J., et al., Evaluation of the influence of in vivo exposure to extremely low-frequency magnetic fields on the plasma levels of pro-inflammatory cytokines in rats, *International Journal of Radiation Biology*, (2018), 1-28. DOI: 10.1080/09553002.2018.1503428
- [32] Karve I.P., Taylor J.M., Crack P.J., The contribution of astrocytes and microglia to traumatic brain injury," *British Journal of Pharmacology*, 173 (2016), No. 4, 692-702.
- [33] Rothhammer V., Quintana F.J., Role of astrocytes and microglia in central nervous system inflammation, *Semin. Immunopathol.*, 37 (2015), No. 6, 575-576.
- [34] Consoles C., et al., Electromagnetic Fields, Oxidative Stress, and Neurodegeneration, *International Journal of Cell Biology*, (2012), Art. No. 683897, 1-16.
- [35] Arendash G.W., et al., Electromagnetic Treatment to Old Alzheimer's Mice Reverses β -Amyloid Deposition, Modifies Cerebral Blood Flow, and Provides Selected Cognitive Benefit, *PLoS One*, 7 (2012), No. 4, Art. No. e3575.
- [36] Arendash G.W., et al., Electromagnetic Field Treatment Protects Against and Reverses Cognitive Impairment in Alzheimer's Disease Mice, *Journal of Alzheimer's Disease*, 19 (2010), No. 1, 191-210.
- [37] George M.S., Stimulating the brain, *Scientific American*, 289 (2003), No. 3, 66-73.
- [38] Greenebaum B., et al., Effects of pulsed magnetic fields on neurite outgrowth from chick embryo dorsal root ganglia, *Bioelectromagnetics*, 17 (1996), No. 4, 293-302.
- [39] Mostert S., Kesselring J., Effect of pulsed magnetic field therapy on the level of fatigue in patients with multiple sclerosis – A randomized controlled trial, *Multiple Sclerosis Journal*, 11 (2005), No. 3, 302-305.
- [40] Sieroń A. (Ed.), *Zastosowanie pól magnetycznych w medycynie*, Alfa-Medica Press, (2002).
- [41] Krawczyk A., et al., Healing of orthopaedic diseases by means of electromagnetic field, *Przegląd Elektrotechniczny*, 86 (2010), No. 12, 72-74.
- [42] Miaskowski A., Krawczyk A., Ishihara Y., Computer modelling of magnetotherapy in orthopedic treatments. *COMPTEL-The International Journal for Computation and Mathematics in Electrical and Electronic Engineering*, 29 (2010), No. 4, 1015-1021.
- [43] Cieśla A., Kraszewski W., Skowron M., Syrek P., Analiza rozkładu pola magnetycznego generowanego przez urządzenia do fizykoterapii, *Przegląd Elektrotechniczny*, 91 (2015), No. 2, 162-165.
- [44] Gryz K., et al., Narażenie na pole elektromagnetyczne w otoczeniu aplikatorów urządzeń magnetoterapeutycznych, *Probl. Hig. Epidemiol.*, 96 (2015), No. 3, 578-585.
- [45] Madkan A., et al., Steps to the clinic with ELF EMF, *Natural Science*, 1 (2009), No. 3, 157-165.
- [46] Pasek J., et al., Zastosowanie pola magnetycznego oraz promieniowania optycznego w leczeniu zespołów bólowych kręgosłupa, w szczególności rwy kulszowej, *Aktualności Neurologiczne*, 12 (2012), No. 1, 65-68.
- [47] Pilla A.A., Nonthermal electromagnetic fields: from first messenger to therapeutic applications, *Electromagnetic Biology and Medicine*, 32 (2013), No. 2, 123-136.
- [48] Sieroń A., Cieślar G., Application of variable magnetic fields in medicine-15 years experience, *Wiadomości Lekarskie* 56 (2003), No. 9-10, pp. 434-441 [in Polish].
- [49] Sandyk R., Treatment with electromagnetic fields reverses the long-term clinical course of a patient with chronic progressive multiple sclerosis, *International Journal of Neuroscience*, 90 (1997), No. 3-4, 177-185.
- [50] Bersani F.S., et al., Deep transcranial magnetic stimulation as a treatment for psychiatric disorders: A comprehensive review, *European Psychiatry*, 28 (2013), No. 1, 30-39.
- [51] Cummings J.L., Progress in Neurotherapeutics and Neuropsychopharmacology 2007, *Progress in Neurotherapeutics and Neuropsychopharmacology*, 2 (2007), No. 1, 1-12.
- [52] Zyss T., *Magnetotherapy*, *Neuro Endocrinology Letters*, 29 (2008), Suppl 1, 161-201.
- [53] Klein M.M., et al., Transcranial magnetic stimulation of the brain: guidelines for pain treatment research, *Pain*, 156 (2015), No. 9, 1601-1614.
- [54] Philpott A.L., et al., Transcranial magnetic stimulation as a tool for understanding neurophysiology in Huntington's disease: A review, *Neuroscience & Biobehavioral Reviews*, 37 (2013), No. 8, 1420-1433.
- [55] Arendash G.W., Review of the Evidence that Transcranial Electromagnetic Treatment will be a Safe and Effective Therapeutic Against Alzheimer's Disease, *Journal of Alzheimer's Disease*, 53 (2016), No. 3, 753-771.
- [56] Arendash G.W., Transcranial electromagnetic treatment against Alzheimer's disease: why it has the potential to trump Alzheimer's disease drug development, *Journal of Alzheimer's Disease*, 32 (2012), No. 2, 243-266.
- [57] Liao X., et al., Repetitive transcranial magnetic stimulation as an alternative therapy for cognitive impairment in Alzheimer's disease: a meta-analysis, *Journal of Alzheimer's Disease*, 48 (2015), No. 2, 463-472.
- [58] Starzynski J., et al., Simulation of magnetic stimulation of the brain, *IEEE Transactions on Magnetics*, 38 (2002), No. 2, 1237-1240.
- [59] Miaskowki A., Krawczyk A., Łada-Tondyry E., Electromagnetic field in transcranial magnetic stimulation, *Przegląd Elektrotechniczny*, 90 (2014), No. 12, pp. 244-246.
- [60] Syrek P., Barbulescu R., Parametric curves to trace the TMS coils windings, *2017 10th International Symposium on Advanced Topics in Electrical Engineering (ATEE)*, (2017), Art. No. 7905069, 386-391. DOI: 10.1109/ATEE.2017.7905069