Archives Italiennes de Biologie, 145: 1-12, 2007.

NEUROBIOLOGICAL EFFECTS OF MICROWAVE EXPOSURE: A REVIEW FOCUSED ON MORPHOLOGICAL FINDINGS IN EXPERIMENTAL ANIMALS

J. ORENDÁČOVÁ[1], M. ORENDÁČ[2], E. RAČEKOVÁ[1] AND J. MARŠALA[1]

[1] Institute of Neurobiology, Center of Excellence, Slovak Academy of Sciences, Košice, Slovak Republic; [2] Faculty of Electrical Engineering and Informatics, Department of Theoretical Electrotechnics and Electrical Measurement, Technical University of Košice, Slovak Republic

INTRODUCTION

All life on the Earth has adapted to survive in an environment of weak natural electromagnetic fields (EMF) which came from two main sources: sun and thunderstorm activity. But in the last hundred years this natural EMF background has been altered by man-made energy sources. The man-made energy sources generate electromagnetic waves, which can be characterized by their wavelength, frequency or intensity and power. Electromagnetic waves at high frequencies are called electromagnetic radiation (EMR) or radio-frequency radiation (RFR). Radiofrequency fields (RFF) at high frequencies in the GHz range are microwaves. The main sources of RFR are e.g. radio, television, radar, cellular telephones antennas and microwave ovens. This scale of frequencies physically belongs to "non-ionizing" radiation range. Thus, exposure of living organisms to the EMR is not a new phenomenon but during the last hundred years environmental exposure to man-made EMF has been steadily increased and in the modern era everyone is exposed to a complex mix of EMF at much higher intensities than whenever before.

Concerns about a possible health effect of RFR energy go back to the Second World War and before, and reports of health effects appeared in the Soviet and Eastern European literature in the 1950s and 1960s (13). The possible risk of microwave radiation, in GHz range, for the nervous system has been regularly published for at least 40 years, when radar and microwave cookers posed a possible health problem, i.e. before the beginning of the mobile phones expansion (7, 8).

This review is focused on neuro-morphological methods and results achieved on various animals in defined laboratory conditions, mimicking the environment polluted by RFR energy rather than the related physical data of experiments.

BIOLOGICAL EFFECTS OF RFR

The term "biological effect" is used to refer changes of a physiological, biochemical or behavioral nature, which are induced in an organism, tissue or cell, in response to

Corrisponding author: MUDr. Judita Orendáčová, PhD. Institute of Neurobiology, Center of Excellence, SAS, šoltésovej 4,040 01 Košice, Slovak Republic. Phone: +421-55-678 50 64, Fax: +421-55-678 50 74, E-mail: orendac@saske.sk

external stimulation. A "biological effect" only becomes a safety hazard when it causes a detectable impairment of an individual's health or health of her or his offspring. A "health effect" is a biological effect, which may endanger the normal working of an organism to this stimulation in that it goes beyond the framework of the physiological responses to the action of the external factor. It is known that the absorbed RFR is converted into heat. Tissue heating or "thermal" effect can occur in tissue as a result of EMF absorption in the dissipative tissue media. The absorbed RF energy in tissue is quantified by using the specific absorption rate – SAR (W/kg), which is the primary parameter used when discussing the health risk due to the EMF power absorption in the body, or using the maximum permissible exposure value, which is the upper limit of RFR power density (W/m^2) exposure for biological tissues (for details about SAR calculation see 27). Thermal effects have been studied extensively in cells and animals, and it has been known for many years that exposure to very high levels of RFR can be harmful due to the ability of RF energy rapidly heat biological tissue. Consequently, biological systems alter their functions as a result of change in temperature (23). On the other hand "non-thermal" effects are not caused by heat, but by direct interaction of the RFF with molecules and tissue components and till now are not very well understood.

Speculations that the biological responses of animal and human bodies to RFR are actually stress responses, i.e. that the RFR is a stressor, started Lai in 1987 (21). The same author a few years later, put some evidence on similar effects of the RFR and stress reaction and in this light the RFR started to be considered a potential health hazard (24, 25, 22). It was shown that RFR activates the stress hormone, corticotropin releasing factor, and affects benzodiazepine receptors in the brain, i.e. the mediators known to change when an animal is stressed (for review of the stress related disorders see 35). That is why the EMR is sometimes referred as an agent of electrostress.

RFR EFFECTS ON NERVOUS TISSUE

Biophysical relations of the RFR on nervous tissue can be consistently and clearly expressed by Weinberger and Richter's (44) article title: "Cellular telephones and effects on the brain: The head as an antenna and brain tissue as a radio receiver". The effect of RFF on extraordinarily complex nervous system is widely discussed in scientific papers, popular journals and on internet. WHO Regional Office for Europe introduced that approximately 25,000 articles have been published in the area of biological effects and medical applications of non-ionizing radiation till 1996. In comparison to the huge number of wide range of literary data and reviews of them, the literary reviews dealing only with the microwave effects on the nervous systems are much more less.

Recently a couple of comprehensive reviews about the effects of RMR appeared: the epidemiological review of D'Andrea *et al.*, (9), review of Hossmann and Hermann (15) about multidisciplinary experimental studies and mini-review of Westerman and Hocking (45) on case reports of RFR effects on the peripheral nervous system. The latest review article of Karger (19), on raised public concern about the possibility of associated adverse health effects of mobile phone technology, shows that there is currently some evidence for its biological effects but further high-quality research is still necessary.

It should be pointed out that although the research in this field spans the disciplines of physics and engineering, biophysics, molecular genetics, clinical and ecological studies, the voluntary exposure of the human brain to microwaves from hand-held mobile phones by approximately one-fourth of the world population can be called "the largest human biological experiment ever". Without any doubt EMF, due to the mobile phones, which are on the best way to become "cigarettes of this century", appeared as a new serious public health issue. One of the key points, on the way of establishing potential health hazard of EMR, represents laboratory studies on animals and among them systematic neuro-morphological studies represent a basis for all other scientific fields.

MORPHOLOGICAL STUDIES ON EXPERIMENTAL ANIMALS AFTER RFR

Our review of the literary data about EMR experiments on animals shows that rat is the most often used animal in such experiments and the blood-brain barrier (BBB) is one of the first and the most studied morpho-functional unit of nervous tissue in this field (Table I).

The BBB changes

Since in 1977, Oscar and Hawkins (33) demonstrated temporary changes in the permeability for small molecular weight saccharides in the BBB system of rats for the first time, leakage of many other tracers was published in connection with EMR in experimental animals (29, 2, 6, etc.).

At the same time some contradictory results have been published. Preston *et al.* (34) and Lin and Lin (26) demonstrated absence of the BBB increased permeability for ^{14}C–manitol and/or sodium fluorescein in animals exposed to the EMR. Gruenau *et al.* (14), and later Ward and Ali (43), by using of ^{14}C-sucrose, as well as ^{3}H-inulin, after microwave irradiation of rats, showed no leakage of the tracers, regardless of the microwaves power density level. They concluded that there is no damage of BBB after such intervention.

Heating/cooling effects on BBB permeability

The thermal controls, i.e. samples subjected to direct heating, have been studied beside the microwave exposure from the beginning of the experimental studies on animals. Merritt *et al.* (29), to replicate the initial investigations on BBB (of the above mentioned Oscar and Hawkins, 33), studied brain uptake of parenterally administered fluorescein and ^{14}C-manitol isotope after similar exposure of rats. Increased fluorescein uptake was seen only when the rats were made hyperthermic in a warm-air environment. The attempts to alter permeability of BBB for manitol-

Table 1. - *Studies on BBB permeability after microwave exposure: a chronological view of selected papers.*

Authors	Experimental conditions	Results
Oscar and Hawkins 1977	Single 20 min exposure to 1.3 GHz; pulsed or continuous waves. D-mannitol Rats	Nonuniform leakage, in medulla, cerebellum,hypothalamus, hippocampus and cerebral cortex observed immediately and 4 h after exposure, but not later.
Merritt *et al.* 1979	Replicated Oscar and Hawkins's (1977) study in combination with direct heating; Fluorescein and ^{14}C-manitol	Increased fluorescein uptake only in a warm-air environment. The brain must be "made hyperthermic" to occur changes induced by microwave radiation.
Albert and Kerns 1981	Low-level microwaves HRP Chinese hamster	Reversible increasing of BBB permeability and lesions in random brain areas.
Arber *et al.* 1986	Single 60 min exposure to 2450 MHz; Helix aspersa	EM changes in the Golgi complex and swelling of endplasmic reticulum in neurons of subesophageal ganglia.
Neilly and Lin 1986	15 min exposure to 3.15 GHz combined with ethanol administration; Evans blue; Rats	Ethanol inhibits microwave-induced permeation of the BBB by reduced heating of the brain. Increased ethanol quantity decreased degree of brain tissue staining.
Salford *et al.* 1992; 1993; 1994	Subthermal power density (pulse modulated and continuous); Rats	Albumine leakage from capillaries and its accumulation in the brain neurons and glial cells was proved in series of 1600 rats.
Ikeda *et al.* 1994	8 MHz; Evans blue; Dogs	BBB breakdown and histological changes of neurons and myelinated fibres at 43 °C.
Fritze *et al.* 1997	4 h exposure to the SAR of 7.5 W/kg; Rats	Only in this experimental group very modest reversible extravasation.
Salford *et al.* 2003	2 h exposure to the SAR of 2, 20, and 200 mW/kg and 50 days survival; Rats	Cresyl violet and albumin antibody showed neuronal damage in the cortex, hippocampus and basal ganglia.

C^{14} or fluorescein only with EMR were unsuccessful. These studies indicated that the brain must be made hyperthermic to occur changes in permeability of the BBB induced by microwave radiation (29).

There are some studies demonstrating that the model of BBB can be utilized also for demonstration of the microwaves heating effects. Neilly and Lin (30) published combined effect of ethanol and microwaves on BBB penetration for Evans blue in anesthetized rats. The results showed that as the quantity of ethanol was increased, the degree of brain tissue staining was decreased or eliminated. This study indicates that ethanol inhibits microwave-induced permeation of the BBB through reduced heating of the brain.

Ikeda *et al.* (16) demonstrated the BBB breakdown for Evans blue and histological changes of neurons and myelinated fibres as a thermal effect of RFR in dog brain at 43 °C. In agreement with these results, Ohmoto *et al.* (31) observed significant histological changes and cerebral blood flow increase in the brain cortex, heated between 41 °C and 43 °C.

On the other hand, different morphological findings in "heat controls" used in RFR paradigm (18, 40, 10) were taken into account of the RFR non-thermal effects. However, Lai (23) disagree with such interpretation because it is difficult to reproduce the pattern of RFR internal heating by an external heating, as it is known that a conventional oven cooks food in a different way than a microwave oven. Thus, the results that "heat control do not produce the same effect of RFR", does not really support the existence of non-thermal effects (23).

Histological findings beside the BBB changes

Albert and Kerns published in 1981 (21) a reversible increase of BBB permeability to horseradish peroxidase (HRP) after low-level microwave exposure of Chinese hamster. Beside these changes they demonstrated also lesions in random areas of the brain immediately following exposure. The lesions were not as common following 1 hr recovery period, and were absent after 2 hrs recovery period.

Among the morphological observations after animal exposure to the EMR are electron microscopical findings very rare but the submicroscopical observations started very early. Arber *et al.* (6) demonstrated minor changes in Golgi complexes and slight swelling of endoplasmic reticulum of snail neurons.

The observations of Salford's research team started a new era of EMR experimental work – the mobile phone era. His team in series of more than 1600 rats, has proven that subthermal power density from both pulse-modulated and continuous RFF including those from GSM (Global System for Mobile Communications) mobile phones have the potency to significantly open the BBB such that the animal's own albumin (but not fibrinogen) passes out of the blood stream into the brain tissue and accumulates in the neurons and glial cells surrounding the capillaries (36, 37, 38).

Fritze *et al.* (12) described a very modest reversible extravasation of albumin after microwave exposure without any histological injury observed in rat brain tissues.

Recently, Salford *et al.* (39) has taken a different approach to focus on the possibility that microwave exposures causing BBB damage could cause damage to the brain itself. In this study 12-26 weeks old rats were chosen because their developmental age is comparable to that of human teenagers, notably the most frequent users of mobile phones. Paraffin sections were stained for RNA/DNA with cresyl violet to show "dark" neurons and albumin antibody to reveal albumin. A highly significant ($p < 0.002$) evidence for neuronal damage, i.e. presence of "dark" neurons, in the cortex, hippocampus, and basal ganglia, in the brains of exposed rats was found. Some of these "dark" neurons were also albumin positive. In spite of the results, the authors opinion is that this kind of neuronal damage may not have immediately demonstrable consequences, even if repeated but in the long run it may result in reduced brain reserve capacity, that might be unveiled by other later neuronal disease or aging.

Histopathological findings

Albert and DeSantis in 1975 (1) published that microwave irradiation of Chinese hamsters consistently selectively alters some areas of the CNS (Table II). At the microscopic level, neuronal somata in the hypothalamus and subthalamus displayed vacuolisation and chromatolysis. The Fink-Heimer technique has provided some tentative evidence that microwave irradiation may produce axonal degeneration. Electron microscopy revealed a decrease in the protein synthesis apparatus, i.e. scarcity of rough endoplasmic reticulum and polyribosomes, and presence of swollen membranous structures in hypothalamic neuropil dendrites.

A couple of articles appeared on effect of non-ionizing radiation on cerebellum. Pregnant squirrel monkeys, exposed to RFR from the beginning of pregnancy till the offspring's first 9.5 months, showed no significant differences between control and experimental animals in the number of Purkinje cells (3). Another study of these authors was done on rats (4) exposed to microwaves at various ages as well as during pregnancy. Quantitative studies of Purkinje cells showed a significant and irreversible decrease in rats irradiated during fetal or fetal and early postnatal life. In animals exposed postnatally, and euthanized immediately after irradiation, significant decrease in the relative number of Purkinje cells was apparent.

Light and electron microscopical study of neonatal rats cerebella (5) revealed the presence of small deeply stained cells with hyperchromatic pycnotic nuclei within

Table 2. - *Morphological findings after microwave exposure: a chronological view of selected papers.*

Authors	Methods and animals	Results
Albert and DeSantis 1975	Fink-Heimer degeneration technique; Electron microscopy; Chinese hamster	Vacuolisation and chromatolysis in neurons of hypo- and subthalamus. Axonal degeneration. Scarcity of rough endoplasmic reticulum and polyribosomes.
Albert *et al.* 1981	Quantitative study; Squirrel monkey	Irreversible decrease of Purkinje cells immediately after irradiation.
Albert and Sheriff 1988	Light and electron microscopy; Neonatal rats	Pycnotic nuclei in external granular layer of the cerebellum, clumped chromatin, membrane disintegration.
Mausset *et al.* 2001	Semiquantitative GABA immunohistochemistry; Rats	Decrease in optical density in the all three layers of cerebellum immediately after exposure.
Takahashi *et al.* 2002	Histopathology; Ki-67; Big blue mice	Negative results about gliosis, degenerative lesions and apoptosis.

the external granular layer. The number of these cells in the exposed rats was nearly twice that in the controls. The Nissl bodies in Purkinje cells were finely dispersed and in some experimental animals mononuclear cellular infiltration was visible. Under electron microscope the deeply stained pycnotic small cells presented electron dense nuclei with clumped chromatin, extrusion or disintegration of the nucleus, ruptured nuclear membrane, and vacuolization of the cytoplasm. Most of the Purkinje cells of experimental animals showed small, disorderly arrays of rough endoplasmic reticulum instead of typical orderly stacks of parallel arrays. The authors suggest that microwave radiation may interfere with early genesis of cerebellar neurons and alter the metabolic status of Purkinje cells.

Immunohistochemical and histochemical findings

Semiquatitative immunohistochemical analysis was used to investigate the effects of RFR on cerebellar neurotransmitter GABA content (28) in rats. Selective diminution of the stained processes area in the Purkinje cell layer after exposure to pulse RFR and, in addition, a decrease in optical density in the all three cell layers after exposure to continuous RF waves were demonstrated.

The possible mutagenic potential of EMR was investigated in locally exposed Big blue mice brain (42). No gliosis or degenerative lesions were histopathologically noted in the brain tissues, and no obvious differences in Ki-67 labeling and apoptotic increases of glial cell were evident.

Contemporary morphological findings

In this chronological setting of literary data it is interesting to mention the latest results from studies testing the effects of the EMF on experimental animals published in 2005 (Table III). The BBB is still an object of research interest however, at the level of genes related to the alteration of this structure (20). After local, head exposure of immature (4 weeks old) rats, equivalent in age to the time when the BBB development is completed, and young adult rats, respectively, there were no pathological changes of vascular permeability, monitored with reference to the transfer of FITC-dextran and FC20.

An associated study of acute effects of pulsed microwaves and 3-nitropropionic acid on neuronal ultrastructure in the rat caudate-putamen showed that the microwave exposure changed neuronal ultrastructure in ways that depends on microwave SAR and neuron metabolic status (41).

Finnie (11) studied the effect of acute exposure to GSM on immediate early gene, c-fos expression in mice brain. Using a purpose-designed exposure system, mice were given a single whole body exposure. Control mice were sham-exposed or freely mobile in cage without further restrain. The c-fos protein expression was detected immunohistochemically in perfusion-fixed brains. Activation of c-fos in the exposed and sham-exposed brains was comparable, but was greatly increased in comparison to the freely moving controls. These results suggest that the majority of acute genomic response detected by c-fos expression was due to immobilization rather than irradiation.

Table 3. - *Neuro-morphological studies of EMR published in 2005.*

Authors	Methods and animals	Results
Kuribayashi *et al.* 2005	Genes related to the BBB alteration; Immature and young adult rats	No pathological relevant differences for FITC and FD20 tracer after local head exposure in immature and young adult animals.
Seaman and Phelix 2005	EM quantitative study; Rats	Ultrastructural changes in neurons are dependent on metabolic status of neurons and microwave SAR.
Finnie 2005 mals	c-fos immunohistochemistry; Mice	Activation of c-fos in the irradiated ani- is rather due to their immobilization than due to the applied irradiation.
Inouye *et al.* 2005	Quantitative analysis; Golgi-Cox impregnation; Rats	Intrauterine and early postnatal irradiation of animals does not influence brain development.
Orendacova *et al.* 2005	Fluoro Jade-B and NADPHd histochem.; HSP immunohistoch.; Rats	Neurogenetic regions of aged animals are more sensitive to the EMR than the regions of adult animals.

In a developmental study of male Sprague-Dawley rats (17) exposure of animals started from prenatal period (in utero exposure) till day 40 postpartum. The histological parameters examined included the brain cortex architecture, germinal layer along the lateral ventricles and the myelination of corpus callosum. Quantitative measurement of neurons, the spine density of the pyramidal cells in layer III of the somatosensory cortex and the density of basal dendritic trees of the pyramidal cells in layer V were measured in Golgi-Cox impregnated specimens. The density of Purkinje cells was measured in the thionin stained specimens. The published data from this study, in spite of their impact on various brain structures and age of animals, also failed to demonstrate that there is a significant effect on the rat brain development due to microwave exposure during the embryonic, fetal and postnatal period.

The microwave effect on neurogenetic region related to the olfactory system in young adult and aged rats (32) was evaluated. The animals were irradiated with a pulsed-wave RFF for 8 hrs. After 24 hrs and 4 weeks survival NADPH-diaphorase and Fluoro Jade-B histochemistry and HSP immunohistochemistry were performed. The results indicate that the rostral migratory stream and subventricular zone in the aged rats is more sensitive for the RFF than in the young adult animals. This comparative study deals with evaluation of cell proliferation and migration changes due to the known neurodegenerating agent – alcohol, and potentially neurodegenerating agent – the EMR.

CONCLUSION

This review shows that despite of many studies, the evidence for microwave health hazard remains controversial. The morphological findings in experimental animals put some evidence on nervous tissue structural damage after RFR exposure, but the results are ambiguous and very often vague. In our opinion, disclosing changes in nervous tissue due to the RFR needs standard well defined laboratory conditions, mimicking environment polluted by RFR energy, and using a vide range of contemporary neuromorphological methods. Collaboration between engineers, biologists and medical professionals is highly expected.

SUMMARY

The possible risk of electromagnetic radiation (EMR) for nervous system is regularly published from the middle of 20th century. Numbers of neurobiological studies demonstrate that various EMR frequencies induce changes in nervous tissue of experimental animals but the evidence for health effect of EMR to the nervous system remains uncertain. To solve the fundamental questions about possible health hazard of modern technologies, the main producers of EMR, further intensive experimental studies on animals are needed.

This review, focused on morphological findings achieved in various experimental animals, demonstrates that blood-brain barrier is the most studied morpho-functional unit of CNS in experiments with EMR. The morphological findings in experimental animals, in many cases controversial, put some evidence on nervous tissue structural damage after the EMR exposure. In spite of numerous literary data a wide range of contemporary neuro-morphological methods waits to be utilized in the EMR experimental paradigm. Using these methods could play an important role in answering the question about possible adverse effects of microwaves on nervous system.

Acknowledgements. - This work was supported by the VEGA grants: 2/5135/25 and 2/6213/26.

REFERENCES

1. ALBERT, E.N. AND DESANTIS, M. Do microwaves alter nervous system structures? *Annal. NY Acad. Sci.,* **247**: 87-108, 1975.
2. ALBERT, E.N. AND KERNS, J.M. Reversible microwave effects on the blood-brain barrier. *Brain Res.,* **230**: 153-164, 1981.
3. ALBERT, E.N., SHERIF, M.F. AND PAPADOPOULOS, N.J. Effect of nonionizing radiation on the Purkinje cells of the uvula in squirrel monkey cerebellum. *Bioelectromagnetics,* **2**: 241-246, 1981.
4. ALBERT, E.N., SHERIF, M.F. AND PAPADOPOULOS, N.J. Effect of nonionizing radiation on the Purkinje cells of the rat cerebellum. *Bioelectromagnetics,* **2**: 247-257, 1981.
5. ALBERT, E.N. AND SHERIF, M. Morphological changes in cerebellum of neonatal rats exposed to 2.45 GHz microwaves. *Progr. Clin. Biol. Res.* **257**: 135-151, 1988.
6. ARBER, S.L., NEILLY, J.P., LIN, J.C. AND KRIHO, V. The effect of 2450 MHz microwave

radiation on the ultrastructure of snail neurons. *Physiol. Chem. Phys. Medical NMR,* **18**: 243-249, 1986.

7. Baranski, S. and Edlwejn, Z. Electroencephalographic and morphological investigations on the influence of microwaves on the central nervous system. *Acta Physiol. Pol.,* **18**: 517-532, 1967.
8. Baranski, S. and Edlwejn, Z. Studies on the combined effect of microwaves and some drugs on bioelectric activity of the rabbit nervous system. *Acta Physiol. Pol.,* **19**: 31-41, 1968.
9. D'andrea, J.A., Chou, C.K., Johnston, S.A. and Adair, E.R. Microwave effects on the nervous system. *Bioelectromagnetics,* **24** (Suppl): 107-147, 2003.
10. D'inzeo, G., Bernardi, P., Eusebi, F., Grassi, F., Tamburello, C. and Zani, B.M. Microwave effects on acetylcholine-induced channels in cultured chick myotubes. *Bioelectromagnetics,* **9**: 363-372, 1988.
11. Finnie, J.W. Expression of the immediate early gene, c-fos, in mouse brain after acute global system for mobile communication microwave exposure. *Pathology,* **37**: 231-233, 2005.
12. Fritze, K., Sommer, C., Schmitz, B., Mies, G., Hossmann, K.-A., Kiessling, M. and Wiessner, C. Effect of global system for mobile communication (GSM) microwave exposure on blood-brain barrier permeability in rat. *Acta Neuropathol.,* **94**: 465-470, 1997.
13. Goldberg, R.B. Literature resources for understanding biological effects of electromagnetic fields. *EMF – Link, http://infoventures.com* 1996.
14. Gruenau, S.P., Oscar, K.J., Folker, M.T. and Rapoport, S.I. Absence of microwave effect on blood-brain barrier permeability to [^{14}C]sucrose in the conscious rat. *Exp. Neurol.,* **75**: 299-307, 1982.
15. Hossmann, K.-A. and Hermann, D.M. Effects of electromagnetic radiation of mobile phones on the central nervous system. *Bioelectromagnetics,* **24**: 46-62, 2003.
16. Ikeda, N., Hayashida, O., Kameda, H., Ito, H. and Matsuda, T. Experimental study on thermal damage to dog normal brain. *Int. J. Hyperther.,* **10**: 553-561, 1994.
17. Inouye, M., Galvin, M.J. and Mcree, D.I. Effect of 2,450 MHz microwave radiation on the development of the rat brain. *Teratology,* **28**: 413-419, 2005.
18. Johnson, C.C. and Guy, A.W. Nonionizing electromagnetic wave effect in biological materials and systems. *Proc. IEEE,* **60**: 692-718, 1971.
19. Karger, C.P. Mobile phones and health: A literature overview. *Z. Med. Physik,* **15**: 73-85, 2005.
20. Kuribayashi, M., Wang, J., Fujiwara, O., Doi, Y., Nabae, K., Tamano, S., Ogiso, T., Asamoto, M. and Shirai, T. Lack of effects of 1439 MHz electromagnetic near field exposure on the blood-brain barrier in immature and young rats. *Bioelectromagnetics,* **26**: 578-588, 2005.
21. Lai, H. Acute exposure to noise affects sodium-dependent high-affinity choline uptake in the central nervous system of the rat. *Pharmacol. Biochem. Behav.,* **28**: 147-151, 1987.
22. Lai, H. Research on the neurological effects of nonionizing radiation at the University of Washington. *Bioelectromagnetics,* **13**: 513-526, 1992.
23. Lai, H. Neurological effects of radiofrequency electromagnetic radiation. Mobile Phone and Health symposium, Vienna, *http://www.mapcruzin.com* 1998.
24. Lai, H. and Carino, M.A. Acute white noise exposure affects the concentration of benzodiazepine receptors in the brain of the rat. *Pharmacol. Biochem. Behav.,* **36**: 985-987, 1990.
25. Lai, H., Carino, M.A., Horita, A. and Guy, A.W. Corticotropin-releasing factor antagonist blocks microwave-induced changes in central cholinergic activity in the rat brain. *Brain Res. Bull.,* **25**: 609-612, 1990.

26. LIN, J.C. AND LIN, M.F. Studies on microwave and blood-brain barrier interaction. *Bioelectromagnetics,* **1**: 313-323, 1980.
27. MARTENS, L., DEMOERLOOSE, J., DEWAGTER, C. AND DEZUTTER, D. Calculation of the electromagnetic fields induced in the head of an operator of a cordless telephone. *Radio Sci.,* **30**: 415-420, 1995.
28. MAUSSET, A.-L., DE SEZE, R., MONTPEYROUX, F. AND PRIVAT, A. Effects of radiofrequency exposure on the GABAergic system in the rat cerebellum: Clues from semi-quantitative immunohistochemistry. *Brain Res.,* **912**: 33-46, 2001.
29. MERRITT, J.H., CHAMNESS, A.F. AND ALLEN, S.J. Studies of blood-brain barrier permeability after microwave-radiation. *Radiat. Envir. Bioph.,* **15**: 367-377, 1978.
30. NEILLY, J.P. AND LIN, J.C. Interaction of ethanol and microwaves on blood-brain barrier of rats. *Bioelectromagnetics,* **7**: 405-414, 1986.
31. OHMOTO, Y., FUJISAWA, H., ISHIKAWA, T., KOIZUMI, H., MATSUDA, T. AND ITO, H. Sequential changes in cerebral blood flow, early neuropathological consequences and blood-brain barrier disruption following radiofrequency-induced localized hyperthermia in the rat. *Int. J. Hyperther.,* **12**: 321-334, 1996.
32. ORENDACOVA, J., RACEKOVA, E., CÌZKOVA, D., FENIK, A., MOJZIS, M. AND ORENDAC, M. *Comparative study of 2.45 GHz radiofrequency fields whole body exposure and alcohol intoxication on neurogenetic region of freely moving rats.* P. 83. In: *Abstracts of 5th International Symposium on Experimental and Clinical Neurobiology.* 2005.
33. OSCAR, K.J. AND HAWKINS, T.D. Microwave alteration of the blood-brain barrier system of rats. *Brain Res.,* **126**: 281-293, 1977.
34. PRESTON, E., VAVASOUR, E.J. AND ASSENHEIM, H.M. Permeability of the blood-brain barrier to mannitol in the rat following 2450 MHz microwave irradiation. *Brain Res.,* **174**: 109-117, 1979.
35. SAAVEDRA, J.M. Brain Angiotensi II: New developments, unanswered questions and therapeutic opportunities. *Cell. Mol. Neurobiol.,* **25**: 485-512, 2005.
36. SALFORD, L.G., BRUN, A., EBERHARDT, J., MALMGREN, L. AND PERSSON, B. *Electromagnetic field-induced permeability of the blood-brain barrier shown by immunohistochemical methods.* Pp. 251-258. In: NORDEN, B., AND RAMEL, C. (Eds.), *Interaction Mechanism of Low-Level Electromagnetic Fields in Living Systems.* Oxford, Oxford University Press, 1992.
37. SALFORD, L.G., BRUN, A., EBERHARDT, J. AND PERSSON, B. Permeability of the blood-brain barrier induced by 915 MHz electromagnetic radiation, continuous wave and modulated at 8, 16, 50, 200 Hz. *Bioelectroch. Bioener.,* **30**: 293-301, 1993.
38. SALFORD, L.G., BRUN, A., STURESSON, K., EBERHARDT, J. AND PERSSON, B. Permeability of the blood-brain barrier induced by 915 MHz electromagnetic radiation, continuous wave and modulated at 8, 16, 50 and 200 Hz. *Microsc. Res. Techniq.,* **27**: 535-542, 1994.
39. SALFORD, L.G., BRUN, A., EBERHARDT, J., MALMGREN, L. AND PERSSON, B. Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones. *Environ. Health Persp.,* **111**: 881-883, 2003.
40. SEAMAN, R.L. AND WACHTEL, H. Slow and rapid responses to CW and pulsed microwave radiation by individual Aplysia pacemakers. *J. Microwave Power EE,* **13**: 77-86, 1978.
41. SEAMAN, R.L. AND PHELIX, C.F. Acute effects of pulsed microwaves and 3-nitropropionic acid on neuronal ultrastructure in the rat caudate-putamen. *Bioelectromagnetics,* **26**: 82-101, 2005.
42. TAKAHASHI, S., INAGUMA, S., CHO, Y.-M., IMAIDA, K., WANG, J., FIJIWARA, O., AND SHIRAI, T. Lack of mutation induction with exposure to 1.5 GHz electromagnetic near fields used for cellular phones in brains of Big blue mice. *Cancer Res.* **62**: 1956-1960, 2002.

43. WARD, T.R. AND ALI, J.S. Blood-brain barrier permeation in the rat during exposure to low-power 1.7-GHz microwave radiation. *Bioelectromagnetics,* **6**: 131-143, 1985.
44. WEINBERGER, Z. AND RICHTER, E.D. Cellular telephones and effects on the brain: The head as an antenna and brain tissue as a radio receiver. *Med. Hypotheses,* **59**: 703-705, 2002.
45. WESTERMAN, R. AND HOCKING, B. Diseases of modern living; neurological changes associated with mobile phones and radiofrequency radiation in humans. *Neurosci. Lett.,* **360**: 13-16, 2004.