# Effect of continuous exposure to alternating magnetic field (50 Hz, 0.5 mT) on serotonin and dopamine receptors activity in rat brain

Branka Janać[1], Gordana Tovilović[2], Mirko Tomić[2], Zlatko Prolić[1] and Lidija Radenović[3]

[1] *Laboratory for Magnetobiology and Behaviour, Institute for Biological Research "Siniša Stanković", University of Belgrade, Bul. Despota Stefana 142, 11060 Belgrade, Serbia*
[2] *Department of Biochemistry, Institute for Biological Research "Siniša Stanković", University of Belgrade, Bul. Despota Stefana 142, 11060 Belgrade, Serbia*
[3] *Department of Physiology and Biochemistry, Faculty of Biology, University of Belgrade, P.O.Box 52, Studentski trg 16, 11000 Belgrade, Serbia*

**Abstract.** External magnetic fields (MFs) have the ability to modify motor activity of animals, complex type of behaviour connected with dopaminergic and serotonergic neurotransmissions in the brain. Thus, the purpose of this study was to examine MF-induced changes in the activity of serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex, as well as dopamine $D_1$ and $D_2$ receptors in the striatum of adult Wistar rats, considering their involvement in motor behavior regulation. Experimental animals were continuously exposed to extremely low frequency MF (ELF-MF, 50 Hz, 0.5 mT) for 1, 3, and 7 days. Subsequently, binding properties ($K_d$ and $B_{max}$) of receptors were determined by *in vitro* radioligand receptor binding assays. It was shown that the affinity of serotonin 5-$HT_{2A}$ receptors decreased and their density increased in the prefrontal cortex of rats after ELF-MF exposure. Regarding affinity, this effect was duration-dependent and most prominent after 7-day of ELF-MF exposure. In contrast to serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex, ELF-MF had no significant effect on the affinity and density of dopamine $D_1$ and $D_2$ receptors in the striatum. We can conclude that continuous exposure to ELF-MF up to 7 days affects cortical serotonergic neurotransmission, whereby intensity of these changes depends on ELF-MF exposure duration.

**Key words:** 50 Hz magnetic field — Serotonin 5-$HT_{2A}$ receptors — Dopamine $D_1$ and $D_2$ receptors — Brain — Rats

## Introduction

Living systems are constantly being exposed to magnetic fields (MFs) of different characteristics (type, frequency, intensity, duration). The natural MF derived from Earth (geomagnetic field) is present during the entire period of living beings evolution, and thus represents a very important ecophysiological factor. Geomagnetic field is under the direct influence of cosmic fields, mostly derived from Sun, which on regular or irregular way change its daily, annual and long-lasting activity. On the other hand, the artificial MFs are unavoidable consequence of impressive scientific and technological development. Among them, alternating MFs of extremely low frequency (ELF, 50–60 Hz) derived from power lines, household appliances, traffic and different industrial technologies deserve particular attention because of their omnipresence in human working and living environment. Magnetic induction values of these MFs are often more pronounced than the values of the natural geomagnetic field (about 20–50 μT in normal conditions).

Numerous experimental and clinical studies indicated that external ELF-MF modify different processes in the brain, including those mediated by serotonergic and dopaminergic neurotransmissions (Lai 1996; Pešić et al. 2004; Janać et al. 2005; Jeong et al. 2006; Jadidi et al. 2007). Even though there are reports that present certain MF effects on serotonergic and dopaminergic neurotransmis-

Correspondence to: Lidija Radenović, Department of Physiology and Biochemistry, Faculty of Biology, University of Belgrade, P.O.Box 52, Studentski trg 16, 11000 Belgrade, Serbia
E-mail: lidijar@bio.bg.ac.rs

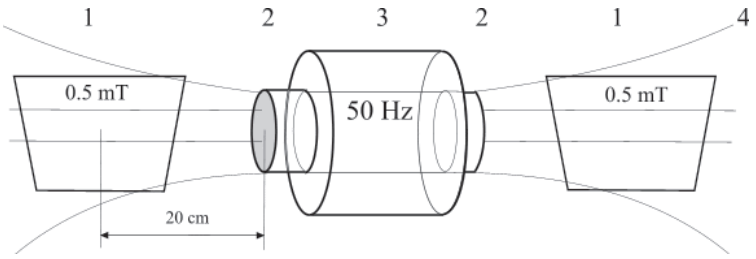


**Figure 1.** Schematic drawing of the MF exposure system. 1 – animal cages; 2 – magnetic poles of ferrite magnetic core; 3 – coils; 4 – magnetic force lines.

sions (Ben-Shachar et al. 1999; Massot et al. 2000; Sieron et al. 2001; Kanno et al. 2003; Sieron et al. 2004), the accurate roles of these neurotransmitter systems in MF-induced changes in the central nervous system (CNS) are not completely explained yet. Thus, the purpose of this study was to investigate effects of continuous ELF-MF (50 Hz, 0.5 mT) exposure for 1, 3, and 7 days on activity (affinity and density) of serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex, as well as dopamine $D_1$ and $D_2$ receptors in the striatum of adult rats. The main reasons for choosing these receptors were our previously published data regarding the effect of MF exposure on animal motor activity and the direct/indirect involvement of serotonin 5-$HT_{2A}$, dopamine $D_1$ and dopamine $D_2$ receptors in motor behavior regulation (Jackson and Westlind-Danielsson 1994; Hillegaart et al. 1996; Janać et al. 2005).

## Materials and Methods

### *Animals*

Adult (about 3-month-old) male Wistar rats, average weight 250–350 g, derived from the vivarium of Institute for Biological Research in Belgrade were used in the research. The animals were housed in groups of 4–5 per cage in standard conditions (room temperature 23 ± 2°C, relative humidity 60–70%, circadian light regime of 12 h, food and water *ad libitum*), according to the principles enunciated in the Guide for Care and Use of Laboratory Animals, NIH publication No. 85-23. They were subjected to experimental protocols approved by the local Ethical Committee.

### *Alternating MF source*

An electromagnet with a regular laminated transformer core and pole diameter of 9.5 cm was used for generation of alternating MF. This electromagnet was supplied with a sinusoidal current (50 Hz, 40 V, 4.5 A), producing relative homogenous ELF-MF with the gradient of magnetic induction. The greatest value of magnetic induction B = 8.9 mT was measured on the electromagnetic poles by a GM05 Gaussmeter (Hirsst) using a PT2837 probe. Magnetic force lines were parallel to the horizontal component of local geomagnetic field. During the experiment, geomagnetic field deviation in the area of study (44°38' N, 20°46' E), measured by a GSM 10 proton magnetometer (Geomagnetic Institute – Grocka, Belgrade), was within the normal range. The background MF did not exceed the value of $10^{-5}$ mT.

### *Experimental procedure*

At the same time, two standard polycarbonate cages (26 cm width × 43 cm length × 15 cm high) with 3–4 experimental animals were placed in the vicinity of ELF-MF source for 1, 3, and 7 days, one on the left and another on the right side of electromagnet (Fig. 1). Cages were placed on polystyrene foam and away from electromagnet to avoid possible vibration and heating. The center of each cage was at 20 cm from the electromagnetic poles and exposed to ELF-MF with an average magnetic induction of B = 0.5 mT. Control animals were submitted to the same experimental procedure with electromagnet turned off (i.e. sham exposed). Animals were sacrificed immediately after the ELF-MF/sham exposure. Dissected prefrontal cortices and corpora striata were weighed and stored at –70°C until biochemical receptor analysis.

Complete set up for ELF-MF exposure system (electromagnet with cages) was in an isolated room with the same values of temperature, relative humidity, artificial light intensity, and circadian light regime as in the vivarium. During continuous exposure to ELF-MF for 1, 3, and 7 days, animals had free access to food and water.

### *Preparation of synaptosomes and saturation binding assay*

Membranes with serotonin 5-$HT_{2A}$ (derived from prefrontal cortex), as well as dopamine $D_1$ and $D_2$ (derived from striatum) binding sites were prepared according to standard

procedures (Vogel 2002). Pooled tissue from three animals was homogenized (6–10 strokes, 800 rpm, Braun homogenizer) in 10 volumes of appropriate ice-cold assay buffer: 50 mmol/l Tris (pH = 7.7; ICN Pharmaceuticals, USA) for cortical, and with salts 50 mmol/l Tris, 120 mmol/l NaCl (Merck), 5 mmol/l KCl (Alkaloid, Skoplje), 2 mmol/l $CaCl_2$ (Merck), 1 mmol/l $MgCl_2$ (pH = 7.5; Merck) for striatal tissue. The homogenate was centrifuged at 40,000 × *g* for 15 min at 4°C (Beckman L7-55 ultracentrifuge, rotor Ti-50). The pellet was re-homogenized in 10 volumes of appropriate assay buffer and re-centrifuged under the same conditions. Finally, sediment was re-suspended in 20 volumes of appropriate assay buffer. Aliquots (~1.5 ml) were stored at –70°C, until use.

*In vitro* saturation binding assays were performed by standard pharmacological procedures described in Vogel (2002). The radioligands used for characterization of serotonin 5-$HT_{2A}$, dopamine $D_1$, and dopamine $D_2$ receptors were [$^3$H]-ketanserin (88 Ci/mmol; Perkin-Elmer, USA), [$^3$H]-SCH23390 (91 Ci/mmol; Amersham, USA), and [$^3$H]-spiperon (77.8 Ci/mmol; Amersham, USA), respectively. Samples in duplicate containing either cortical or striatal membranes and different concentrations (0.25–8 nmol/l for serotonin 5-$HT_{2A}$ receptors; 60 pmol/l–2 nmol/l for dopamine $D_1$ and $D_2$ receptors) of appropriate radioligand were incubated in appropriate assay buffer at 37°C for 10 min. The reaction was terminated by addition of ice-cold buffer and rapid vacuum filtration of the individual samples through Whatman GF/B filters. The filters were washed two times with 3.5 ml of appropriate ice-cold buffer and radioactivity remained on filters was measured using liquid scintillation counter (LKB RackBeta 1219). Nonspecific binding was determined in the presence of 1 μmol/l ketanserin (Sigma Chemical, USA) in case of serotonin 5-$HT_{2A}$ receptors, and 1 μmol/l (+)-butaclamol (Sigma Chemical, USA) in case of dopamine $D_1$ and $D_2$ receptors. Binding of [$^3$H]-spiperon to serotonin 5-$HT_{2A}$ receptors in the striatum was prevented by adding of 50 nmol/l ketanserin to dopamine $D_2$ receptor saturation assay tubes. Protein concentration was determined by the method of Markwell et al. (1978).

### *Statistical analysis*

Values of binding parameters, index of receptor affinity ($K_d$) and index of receptor density ($B_{max}$), of serotonin 5-$HT_{2A}$ receptors, and dopamine $D_1$ and $D_2$ receptors were calculated by GraphPad Prism® software, version 4.00. Results were presented in tables as mean ± SEM of three independent trials each performed in duplicate. One-way ANOVA, followed by post hoc LSD test was used for statistical analysis of obtained data. Results were considered to be significantly different at $p < 0.05$.

## Results

Upon the initial statistical analysis, no significant differences of either affinities or densities of serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex, and dopamine $D_1$ and $D_2$ receptors in the striatum among the three control groups (sham-exposed for 1, 3, or 7 days) were found (data not shown). So, all these data were cumulated and expressed as the only control values. These binding parameters were also found to be in the same range with those reported by the other authors (Papp et al. 1994; Yamada et al. 1995; Gili-Martín et al. 1997).

Activity of serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex of rats was significantly changed after ELF-MF (50 Hz, 0.5 mT) exposure ($K_d - F_{(3,8)} = 11.51$, $p < 0.01$; $B_{max} - F_{(3,8)} = 8.89$, $p < 0.01$; one-way ANOVA). Detail comparisons indicated that ELF-MF reduced the affinity (i.e. increased $K_d$) of serotonin 5-$HT_{2A}$ receptors proportionally to the exposure duration (Table 1A). Alterations were statistically significant after continuous 3- or 7-day ELF-MF exposure. Density of these receptors (i.e. $B_{max}$ value) was significantly increased in the prefrontal cortex of all animals exposed to ELF-MF (Table 1A). Increase in receptor density was not proportional to exposure duration.

In contrast to serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex, ELF-MF exposure irrespective of duration did not significantly modify the affinity or density of dopamine $D_1$ and $D_2$ receptors in the striatum (Table 1B and C). Values obtained for the affinity and density of dopamine $D_1$ receptors of ELF-MF exposed animals were mainly at control levels (Table 1B). On the other hand, a slight tendency toward decreasing of dopamine $D_2$ receptors affinity (i.e. increasing $K_d$) was detected after 1- and 3-day ELF-MF exposure (Table 1C).

## Discussion

The main target of interaction of ELF-MFs on the biological systems is the plasma membrane, namely proteins anchored in lipid bilayer of the cell membrane functioning as ion channels, enzymes, and receptors (Bersani et al. 1997). Some of the proposed mechanisms of ELF-MFs effects are modulations in the receptor/ligand binding, receptor capping, ion transport or overall distribution of the intra-membrane proteins (Adey and Lawrence 1984; Chiabrera et al. 1991a,b; Bersani et al. 1997).

Our results revealed that continuous exposure to ELF-MF (50 Hz, 0.5 mT) for 7 days decreased the affinity of serotonin 5-$HT_{2A}$ receptors and increased their density in the prefrontal cortex of experimental animals. These findings are in accordance with the data of Ben-Shachar et al. (1999), who showed decreased affinity of serotonin 5-$HT_2$ receptors in the frontal cortex of animals after 10 days of

**Table 1.** The effect of continuous exposure to extremely low frequency magnetic field (ELF-MF; 50 Hz, 0.5 mT) for 1, 3, and 7 days on binding parameters (affinity and density) of serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex (A), as well as dopamine $D_1$ and $D_2$ receptors in the striatum (B, C) of experimental animals

**A**

| Serotonin 5-$HT_{2A}$ receptors | | |
|---|---|---|
| Treatment | $K_d$ (nmol/l) | $B_{max}$ (fmol/mg protein) |
| Control | 1.06 ± 0.08 | 57.7 ± 8.3 |
| ELF-MF 1 day | 1.72 ± 0.23 | 81.0 ± 12.0* |
| ELF-MF 3 days | 2.33 ± 0.26** | 94.7 ± 7.5** |
| ELF-MF 7 days | 2.50 ± 0.54** | 71.8 ± 11.8* |

**B**

| Dopamine $D_1$ receptors | | |
|---|---|---|
| Treatment | $K_d$ (nmol/l) | $B_{max}$ (fmol/mg protein) |
| Control | 0.67 ± 0.10 | 128.1 ± 18.2 |
| ELF-MF 1 day | 0.73 ± 0.15 | 112.9 ± 14.0 |
| ELF-MF 3 days | 0.75 ± 0.10 | 110.3 ± 8.5 |
| ELF-MF 7 days | 0.64 ± 0.07 | 155.0 ± 20.9 |

**C**

| Dopamine $D_2$ receptors | | |
|---|---|---|
| Treatment | $K_d$ (nmol/l) | $B_{max}$ (fmol/mg protein) |
| Control | 0.13 ± 0.04 | 87.5 ± 18.5 |
| ELF-MF 1 day | 0.19 ± 0.05 | 68.2 ± 14.0 |
| ELF-MF 3 days | 0.17 ± 0.04 | 84.1 ± 10.6 |
| ELF-MF 7 days | 0.11 ± 0.03 | 96.0 ± 19.2 |

Binding affinities of the receptors for the specific radioligands are represented by the dissociation constants ($K_d$). $B_{max}$ values are the estimated tissue densities of the receptors. Each value represents mean ± SEM of three independent trials performed in duplicate. * $p < 0.05$ and ** $p < 0.01$ indicate significant differences compared to control animals (one-way ANOVA, followed by LSD test).

repetitive transcranial magnetic stimulation treatment. Also, our results are in some way expected, having in mind the role of the serotonergic neurotransmission in the adapted response of the CNS to different external or internal stimulus (Jacobs and Azmitia 1992).

In contrast to serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex, we showed that ELF-MF exposure had no effects on the affinity and density of dopamine $D_1$ and $D_2$ receptors in the striatum of experimental animals. However, we could not exclude the possibility that some changes exist but that they are below the detection level. Sieron et al. (2001) demonstrated reduced reactivity of central dopamine $D_1$ receptors after ELF-MF (10 Hz, 1.8–3.8 mT, 1 h daily) exposure for 14 days in neonatal 6-hydroxydopamine-treated rats. Reasons for this disagreement with our results could arise from differences between animals used and experimental procedures.

Alterations in the affinity and density of serotonin 5-$HT_{2A}$ receptors detected in our experiments could be a direct result of ELF-MF influence on serotonin 5-$HT_{2A}$ receptor protein conformation and/or indirect consequence of ELF-MF-induced changes in serotonin concentration. Massot et al. (2000) already revealed that exposure to a 50-Hz MF in the range of intensity from 0.1 to 1 mT ($EC_{50}$ close to 0.5 mT) specifically affects serotonin 5-$HT_{1B}$ receptors inducing structural changes of the protein and thus functional desensitization of the receptors. At the same time, they did not register effect on serotonin 5-$HT_{2A}$ receptors and possible reasons of this discrepancy with our results could be shorter time period of MF exposure (up to 60 min) and greater susceptibility of serotonin 5-$HT_{1B}$ receptors to the external MF. Concerning serotonin concentration, Sieron et al. (2004) found increase in the synthesis rate (turnover) of serotonin in the frontal cortex of rats after exposure to ELF-MF (10 Hz, 1.8–3.8 mT, 1 h daily) for 14 days. It is known that a quantitative increase in serotonin level at the synaptic cleft may be followed by decreased density of serotonergic receptors in the membrane (Rioux et al. 1999; Li et al. 2000). Having in mind all these facts and results obtained in our study, we consider that direct influence of ELF-MF on serotonin 5-$HT_{2A}$ protein conformation is a more suitable hypothesis for us. In that case, decreased affinity of serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex is the initial event, while increased density of these receptors represents response of the organism on disturbed homeostatic conditions.

Serotonin 5-$HT_{2A}$ receptors are G-protein linked molecules that are positively coupled to phosphoinositide metabolism. They are involved in numerous physiological (motor activity, pain, learning and memory) and pathophysiological (schizophrenia, psychosis, depression, anxiety, migraine) processes in the brain (Hillegaart et al. 1996; Buhot et al. 2000; Naughton et al. 2000; Sandrini et al. 2002). Reported findings already indicated that some of these processes are subjected to modification by external ELF-MFs (Wilson 1988; Lai 1996; Sienkiewicz et al. 1998; Pešić et al. 2004; Janać et al. 2005; Bao et al. 2006; Jeong et al. 2006; Jadidi et al. 2007; Liu et al. 2008). ELF-MF-induced alterations in the activity of serotonin 5-$HT_{2A}$ receptors could affect downstream signal transduction pathways. According to the theory based on the resonance interaction between ELF-MF and intracellular signal cascades (Liboff 1985; Lednev 1991), the effects of MFs on calcium-dependent biological processes provoke extensive consequences in the organisms (Walleczek 1992; Frey 1993). In our previous study we found that exposure to ELF-MF (50 Hz, 0.5 mT) for 7 days reduced amphetamine-induced (1.5 mg/kg, i.p.) motor activity in rats (Janać et al. 2005). It is known that serotonin 5-$HT_{2A}$ receptors are located on the pyramidal (in the large percentage) and GABAergic neurons in the prefrontal cortex (Santana et al. 2004; Wedzony et al. 2008). Also, most of these py-

ramidal neurons are projected to dopaminergic neurons of the ventral tegmental area involved in the control of motor activity (Carr and Sesack 2000). This means that serotonin 5-$HT_{2A}$ receptors in the prefrontal cortex have modulatory influence on dopaminergic activity in the ventral tegmental area and release of dopamine in the mesocortical pathway (Bortolozzi et al. 2005). These facts and our results regarding serotonin 5-$HT_{2A}$ receptors indicate that depressor effect of ELF-MF on amphetamine-induced hypermotor response may be a consequence of reduced mesocortical dopaminergic neurons activity. Moreover, O'Neill et al. (1999) suggested involvement of serotonin 5-$HT_{2A}$ receptors in the behavioral responses induced by compounds that increase synaptic concentration of dopamine, such as amphetamine.

We presume that different effects of ELF-MF on cortical serotonin and striatal dopamine receptors are related to the different threshold of reactions of specific brain regions and/or neurotransmitter systems. Previously reported data support both proposed mechanisms, underlining once again very complex and non-predictable nature of external MFs (Chance et al. 1995; Ben-Shachar et al. 1997; Sieron et al. 2004; Zhang et al. 2005). It is known that the time of the physical and biological reactions have important role in the reaction of the living systems to the MFs. Thus, outcome of an experiment depends on characteristics of applied MF (frequency, intensity, impulse shape, exposure duration) and individual features of the organism (functional state, sex, age).

In conclusion, these results contribute not only to better understanding of mechanism(s) underlying observed motor activity effects, but also to the prediction and explanation of other modifications in the brain processes induced by external ELF-MF.

**Acknowledgement.** This study was supported by the Ministry of Science and Technological Development, Republic of Serbia (grant No. 143027 and 143032).

## References

Adey W. R., Lawrence A. F. (1984): Nonlinear Electrodynamics in Biological Systems. pp. 3–22, Plenum Press, New York

Bao X., Shi Y., Huo X., Song T. (2006): A possible involvement of beta-endorphin, substance P, and serotonin in rat analgesia induced by extremely low frequency magnetic field. Bioelectromagnetics **27**, 467–472

Ben-Shachar D., Belmaker R. H., Grisaru N., Klein E. (1997): Transcranial magnetic stimulation induces alterations in brain monoamines. J. Neural. Transm. **104**, 191–197

Ben-Shachar D., Gazawi H., Riboyad-Levin J., Klein E. (1999): Chronic repetitive transcranial magnetic stimulation alters beta-adrenergic and 5-$HT_2$ receptor characteristics in rat brain. Brain Res. **816**, 78–83

Bersani F., Marinelli F., Ognibene A., Matteucci A., Cecchi S., Santi S., Squarzoni S., Maraldi N. M. (1997): Intramembrane protein distribution in cell cultures is affected by 50 Hz pulsed magnetic fields. Bioelectromagnetics **18**, 463–469

Bortolozzi A., Diaz-Mataix L., Scorza M. C., Celada P., Artigas F. (2005): The activation of 5-$HT_{2A}$ receptors in prefrontal cortex enhances dopaminergic activity. J. Neurochem. **95**, 1597–1607

Buhot M. C., Martin S., Segu L. (2000): Role of serotonin in memory impairment. Ann. Med. **32**, 210–221

Carr D. B., Sesack S. R. (2000): Projections from the rat prefrontal cortex to the ventral tegmental area: target specificity in the synaptic associations with mesoaccumbens and mesocortical neurons. J. Neurosci. **20**, 3864–3873

Chance W. T., Grossman C. J., Newrock R., Bovin G., Yerian S., Schmitt G., Mendenhall C. (1995): Effects of electromagnetic fields and gender on neurotransmitters and amino acids in rats. Physiol. Behav. **58**, 743–748

Chiabrera A., Bianco B., Kaufman J. J., Pilla A. A. (1991a): Quantum dynamics of ions in molecular crevices under electromagnetic exposure. In: Electromagnetics in Medicine and Biology. (Eds. C. T. Brighton and S. R. Pollack), pp. 21–26, San Francisco Press, CA, USA

Chiabrera A., Bianco B., Kaufman J. J., Pilla A. A. (1991b): Quantum analysis of ion binding kinetics in electromagnetic bioeffects. In: Electromagnetics in Medicine and Biology. (Eds. C. T. Brighton and S. R. Pollack), pp. 27–31, San Francisco Press, CA, USA

Frey A. H. (1993): Electromagnetic field interactions with biological systems. FASEB J. **7**, 272–281

Gili-Martín E., Fernández-Briera A., Calvo P. (1997): Effects of chronic ethanol treatment and ethanol withdrawal on [3H]SCH23390 binding to rat striatal membranes. Neuropharmacology **36,** 101–106

Hillegaart V., Estival A., Ahlenius S. (1996): Evidence for specific involvement of 5-$HT_{1A}$ and 5-$HT_{2A/C}$ receptors in the expression of patterns of spontaneous motor activity of the rat. Eur. J. Pharmacol. **295**, 155–161

Jackson D. M., Westlind-Danielsson A. (1994): Dopamine receptors: molecular biology, biochemistry and behavioural aspects. Pharmacol. Ther. **64**, 291–369

Jacobs B. L., Azmitia E. C. (1992): Structure and function of the brain serotonin system. Physiol. Rev. **72**, 165–229

Jadidi M., Firoozabadi S. M., Rashidy-Pour A., Sajadi A. A., Sadeghi H., Taherian A. A. (2007): Acute exposure to a 50 Hz magnetic field impairs consolidation of spatial memory in rats. Neurobiol. Learn. Mem. **88**, 387–392

Janać B., Pešić V., Jelenković A., Vorobyov V., Prolić Z. (2005): Different effects of chronic exposure to ELF magnetic field on spontaneous and amphetamine-induced locomotor and stereotypic activities in rats. Brain Res. Bull. **67**, 498–503

Jeong J. H., Kum C., Choi H. J., Park E. S., Sohn U. D. (2006): Extremely low frequency magnetic field induces hyperalgesia in mice modulated by nitric oxide synthesis. Life Sci. **78**, 1407–1412

Kanno M., Matsumoto M., Togashi H., Yoshioka M., Mano Y. (2003): Effects of repetitive transcranial magnetic stimulation on behavioral and neurochemical changes in rats during an elevated plus-maze test. J. Neurol. Sci. **211**, 5–14

Lai H. (1996): Spatial learning deficit in the rat after exposure to a 60 Hz magnetic field. Bioelectromagnetics **17**, 494–496

Lednev V. V. (1991): Possible mechanism for the influence of weak magnetic fields on biological systems. Bioelectromagnetics **12**, 71–75

Li Q., Wichems C., Heils A., Lesch K. P., Murphy D. L. (2000): Reduction in the density and expression, but not G-protein coupling, of serotonin receptors (5-$HT_{1A}$) in 5-HT transporter knock-out mice: gender and brain region differences. J. Neurosci. **20**, 7888–7895

Liboff A. R. (1985): Geomagnetic cyclotron resonance in living cells. J. Biol. Phys. **13**, 99–102

Liu T., Wang S., He L., Ye K. (2008): Anxiogenic effect of chronic exposure to extremely low frequency magnetic field in adult rats. Neurosci. Lett. **434**, 12–17

Markwell M. A., Haas S. M., Bieber L. L., Tolbert N. E. (1978): A modification of the Lowry procedure to simplify protein determination in membrane and lipoprotein samples. Anal. Biochem. **87**, 206–210

Massot O., Grimaldi B., Bailly J. M., Kochanek M., Deschamps F., Lambrozo J., Fillion G. (2000): Magnetic field desensitizes 5-$HT_{1B}$ receptor in brain: pharmacological and functional studies. Brain Res. **858**, 143–150

Naughton M., Mulrooney J. B., Leonard B. E. (2000): A review of the role of serotonin receptors in psychiatric disorders. Hum. Psychopharmacol. **15**, 397–415

O'Neill M. F., Heron-Maxwell C. L., Shaw G. (1999): 5-$HT_2$ receptor antagonism reduces hyperactivity induced by amphetamine, cocaine, and MK-801 but not $D_1$ agonist C-APB. Pharmacol. Biochem. Behav. **63**, 237–243

Papp M., Klimek V., Willner P. (1994): Parallel changes in dopamine $D_2$ receptor binding in limbic forebrain associated with chronic mild stress-induced anhedonia and its reversal by imipramine. Psychopharmacology (Berl.) **115**, 441–446

Pešić V., Janać B., Jelenković A., Vorobyov V., Prolić Z. (2004): Non-linearity in combined effects of ELF magnetic field and amphetamine on motor activity in rats. Behav. Brain Res. **150**, 223–227

Rioux A., Fabre V., Lesch K. P., Moessner R., Murphy D. L., Lanfumey L., Hamon M., Martres M. P. (1999): Adaptive changes of serotonin 5-$HT_{2A}$ receptors in mice lacking the serotonin transporter. Neurosci. Lett. **262**, 113–116

Sandrini M., Vitale G., Pini L. A. (2002): Central antinociceptive activity of acetylsalicylic acid is modulated by brain serotonin receptor subtypes. Pharmacology **65**, 193–197

Santana N., Bortolozzi A., Serrats J., Mengod G., Artigas F. (2004): Expression of serotonin$_{1A}$ and serotonin$_{2A}$ receptors in pyramidal and GABAergic neurons of the rat prefrontal cortex. Cereb. Cortex **14**, 1100–1109

Sienkiewicz Z. J., Haylock R. G., Bartrum R., Saunders R. D. (1998): 50 Hz magnetic field effects on the performance of a spatial learning task by mice. Bioelectromagnetics **19**, 486–493

Sieron A., Brus R., Szkilnik R., Plech A., Kubanski N., Cieslar G. (2001): Influence of alternating low frequency magnetic fields on reactivity of central dopamine receptors in neonatal 6-hydroxydopamine treated rats. Bioelectromagnetics **22**, 479–486

Sieron A., Labus L., Nowak P., Cieslar G., Brus H., Durczok A., Zagzil T., Kostrzewa R. M., Brus R. (2004): Alternating extremely low frequency magnetic field increases turnover of dopamine and serotonin in rat frontal cortex. Bioelectromagnetics **25**, 426–430

Vogel G. H. (2002): Drug Discovery and Evaluation-Pharmacological Assays. Springer-Verlag, Berlin

Walleczek J. (1992): Electromagnetic field effects on cells of the immune system: the role of calcium signaling. FASEB J. **6**, 3177–3185

Wedzony K., Chocyk A., Maćkowiak M. (2008): A search for colocalization of serotonin 5-$HT_{2A}$ and 5-$HT_{1A}$ receptors in the rat medial prefrontal and entorhinal cortices-immunohistochemical studies. J. Physiol. Pharmacol. **59**, 229–238

Wilson B. W. (1988): Chronic exposure to ELF fields may induce depression. Bioelectromagnetics **9**, 195–205

Yamada S., Watanabe A., Nankai M., Toru M. (1995): Acute immobilization stress reduces (+/–) DOI-induced 5-$HT_{2A}$ receptor-mediated head shakes in rats. Psychopharmacology (Berl.) **119**, 9–14

Zhang J., Wang X., Wang M. (2005): Influence of time-varying magnetic field on the release of neurotransmitters in raphe nuclei of rats. Conf. Proc. IEEE Eng. Med. Biol. Soc. **6**, 6214–6216