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Literature on neurological effects of static and extremely-low frequency electromagnetic fields (2007-2025)

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Keys: (E) - effect observed; (NE) - no significant effect observed.
AS- animal study; CS- cell/in vitro study; CE- chronic/repeated exposure; AE- acute exposure; HU- human study; MC- morphological changes; CC- chemical changes; FC- functional changes; EE- electrophysiological changes; BE- behavioral effect; OX- oxidative changes; DE- development; MA- possible medical application; ND- neurodegenerative disease; EF- electric field; IX- interacts with other entities.

E = 352 (91%); NE = 33 (9%)

Abtin S, Seyedaghamiri F, Aalidaei Z, Farrokhi A, Moshrefi F, Ziveh T, Zibaii ME, Ali akbarian H, Rezaee-Tavirani M, Haghparast A. A review on the consequences of molecular and genomic alterations following exposure to electromagnetic fields: remodeling of neuronal network and cognitive changes. Brain Res Bull 217:111090, 2024. (Review)

The use of electromagnetic fields (EMFs) is essential in daily life. Since 1970, concerns have grown about potential health hazards from EMF. Exposure to EMF can stimulate nerves and affect the central nervous system, leading to neurological and cognitive changes. However, current research results are often vague and contradictory. These effects include changes in memory and learning through changes in neuronal plasticity in the hippocampus, synapses and hippocampal neuritis, and changes in metabolism and neurotransmitter levels. Prenatal exposure to EMFs has negative effects on memory and learning, as well as changes in hippocampal neuron density and histomorphology of hippocampus. EMF exposure also affects the structure and function of glial cells, affecting gate dynamics, ion conduction, membrane concentration, and protein expression. EMF exposure affects gene expression and may change epigenetic regulation through effects on DNA methylation, histone modification, and microRNA biogenesis, and potentially leading to biological changes. Therefore, exposure to EMFs possibly leads to changes in cellular and molecular mechanisms in central nervous system and alter cognitive function.

(E) Acikgoz B, Ersoy N, Aksu I, Kiray A, Bagriyanik HA, Kiray M. GENDER DIFFERENCES IN EFFECTS OF PRENATAL AND POSTNATAL EXPOSURE TO ELECTROMAGNETIC FIELD AND PRENATAL ZINC ON BEHAVIOUR AND SYNAPTIC PROTEINS IN RATS. J Chem Neuroanat 122:102092, 2022. (AS, CE, BE, CC, DE)

Humans are exposed to electromagnetic fields (EMF) from various sources throughout life. Because humans are easily impacted by environmental factors during early development, it is believed that EMF can cause structural and functional changes on the developing brain that may lead to behavioural changes. This paper investigates the impact of EMF exposure and zinc supplementation during the prenatal and postnatal periods on behavioural changes and synaptic proteins in a gender-dependent manner. Pups from four groups of pregnant rats were used: Sham, EMF (5 days/wk, 4h/day EMF-exposure applied), Sham+Zinc (5 days/wk, 5mg/kg/day zinc applied) and EMF+Zinc (5 days/wk, 4h/day EMF-exposure and 5mg/kg/day zinc applied). EMF exposure and zinc supplementation were initiated from the first day of pregnancy to the 42nd postnatal day. Zinc levels in blood, NLGN3 and SHANK3 levels in hippocampus and amygdala, and synaptic structures in amygdala were examined. Behavioural tests showed that EMF exposure had no effect on social behaviour, but adversely affected activity and exploratory behaviour, and led to increased anxiety formation. Zinc supplementation had a partially positive effect on female, but not male offspring. SHANK3 and NLGN3 proteins were significantly lower in EMF groups, however, no positive effect of zinc supplementation was found. In conclusion, EMF exposure may alter the levels of synaptic proteins in the developing brain, leading to behavioural changes in a gender-dependent manner. Evaluation of zinc supplementation at different doses could be beneficial to prevent or reduce the behavioural and structural effects of EMF.

(E) Afrasiabi A, Riazi GH, Abbasi S, Dadras A, Ghalandari B, Seidkhani H, Modaresi SM, Masoudian N, Amani A, Ahmadian S. Synaptosomal acetylcholinesterase activity variation pattern in the presence of electromagnetic fields. Int J Biol Macromol. 65:8-15, 2014. (CS, AE, CC, MA)

Acetylcholinesterase (AChE) is the enzyme that controls the acetylcholine (ACh) concentrations in cholinergic synaptic clefts by hydrolyzing ACh to choline and acetate. Cholinergic synapses are involved in important functions such as learning, memory and cognition. In this study, we investigated the effects of a wide range of extremely low frequency electromagnetic fields (ELF-EMFs) on synaptic ACh concentrations through AChE enzyme activity assay. Synaptosome suspensions were prepared as a neural terminus from cerebral cortex of sheep brain. Prepared synaptosomes were exposed to ELF-EMFs with frequency ranging from 50 Hz to 230 Hz for duration between 15 and 120 min and flux intensity between 0.1 mT and 1.7 mT. Consequently, AChE activity was measured by Ellman method. Raw data were analyzed by neural network based software, Inform 4.02, to predict AChE activity pattern through nine 3D curves. These curves showed that AChE activity decreases when exposed to ELF-EMFs of 1.2 mT to 1.7 mT intensity and 50 Hz to 90 Hz frequency. Thus, it is proposed that exposure to fields of in this range of frequency-intensity would be effective in clinical treatments of cholinergic disorders to increase synaptic ACh concentration. However, more in vivo experiments are needed to develop this suggested treatment.

Aggarwal A, Mendoza-Mari Y, Agrawal DK. Cellular and Molecular Mechanisms and Innovative Neurostimulation Treatments in the Management of Traumatic Brain Injury. J Biotechnol Biomed 7(4):453-470, 2024. (Review)

Traumatic brain injury (TBI) is one of the growing public health problems and a leading cause of disabilities and mortality worldwide. After the mechanical impact to the head, patients of all ages suffer from cognitive and neurological deficits, as well as psychological disorders to different extents. In the last years, the use of electrical impulses and magnetic currents to achieve therapeutic effects have shown promising results and became potential treatments for TBI. Potential mechanisms of action described so far include long term potentiation and depression of neuronal synapses, stimulation of neurotransmitters and growth factors release, and reduction of neuroinflammation, apoptosis and excitotoxicity, among others. Although promising results have been obtained in pre-clinical experiments and limited clinical studies, the high rate of variability in technical parameters and the limited number of patients enrolled have made difficult to clearly define the optimal conditions to obtain reliable therapeutic effects with these stimulation techniques in TBI patients. The present review aims to describe the molecular processes taking place in the brain after the injury, as well as to describe some of the neurostimulation treatments currently under development for TBI management.

(E) Ahmed Z, Wieraszko A. The mechanism of magnetic field-induced increase of excitability in hippocampal neurons. Brain Res. 1221:30-40, 2008. (CS, AE, EE)

The influence of a pulsed magnetic field (PMF) on hippocampal evoked potentials has been investigated in vitro. The exposure to PMF (0.16 Hz, 15 mT) applied for 30 min amplified the population spike and the slope of EPSP recorded from stratum pyramidale and stratum radiatum respectively. This amplification was additive to previously induced LTP and occurred in an NMDA-independent way. The increase in the activity of electrical synapses accompanied PMF-induced amplification of evoked potentials. Since PMF exposure modified paired-pulse facilitation and paired-pulse inhibition, it was concluded that it modifies excitatory and inhibitory processes in the hippocampus. Control experiments revealed that observed effects were exclusively related to PMF exposure. The results support and extend our previous research indicating a significant influence of magnetic fields on hippocampal physiology.

***(B) (MA)* (E) Akbarnejad Z, Esmaeilpour K, Shabani M, Asadi-Shekaari M, Saeedi-Goraghani M, Ahmadi M. Spatial memory recovery in Alzheimer's rat model by electromagnetic field exposure. Int J Neurosci. 128(8):691-696, 2018. (AS, CE, BE, CC, ND, MA)**

INTRODUCTION: Although studies have shown a potential association between extremely low frequency electromagnetic fields (ELF-EMFs) exposure and Alzheimer's disease (AD), few studies have been conducted to investigate the effects of weak magnetic fields on brain functions such as cognitive functions in animal models. Therefore, this study aimed to investigate the effect of ELF-EMF exposure (50 Hz, 10 mT) on spatial learning and memory changes in AD rats. METHODS: Amyloid-β (Aβ) 1-42 (5 μl/ bilateral, single-dose) was injected into lateral ventricle to establish an AD rat model. The rats were divided into six groups: Group I (control); Group II (surgical sham); Group III (AD) Alzheimer's rat model; Group IV (MF) rats exposed to ELF-MF for 14 consecutive days; Group V (Aβ injection+M) rats exposed to magnetic field for 14 consecutive days from day 0-14 days after the Aβ peptide injection; Group VI (AD+M) rats exposed to magnetic field for 14 consecutive days after 2 weeks of Aβ peptide

injection from 14th to 28th day. Morris water maze investigation were implemented and performed 24 h after termination of ELF-MF, respectively. RESULTS: AD rats showed a significant impairment in learning and memory compared to control rats. The results showed that ELF-MF improved the learning and memory impairments in Aβ injection+M and AD+M groups. CONCLUSION: Our results showed that application of ELF-MF not only has improving effect on different cognitive disorder signs of AD animals, but also disrupts the processes of AD rat model formation.

(F) **(E) Akdag MZ, Dasdag S, Ulukaya E, Uzunlar AK, Kurt MA, Taşkin A. Effects of extremely low-frequency magnetic field on caspase activities and oxidative stress values in rat brain. Biol Trace Elem Res. 138(1-3):238-249, 2010. (OX, AS, CC, CE)**

This study was aimed to investigate the effect of extremely low-frequency magnetic field (ELF-MF) on apoptosis and oxidative stress values in the brain of rat. Rats were exposed to 100 and 500 µT ELF-MF, which are the safety standards of public and occupational exposure for 2 h/day for 10 months. Brain tissues were immunohistochemically stained for the active (cleaved) caspase-3 in order to measure the apoptotic index by a semi-quantitative scoring system. In addition, the levels of catalase (CAT), malondialdehyde (MDA), myeloperoxidase (MPO), total antioxidative capacity (TAC), total oxidant status (TOS), and oxidative stress index (OSI) were measured in rat brain. Final score of apoptosis and MPO activity were not significantly different between the groups. CAT activity decreased in both exposure groups ($p < 0.05$), while TAC was found to be lower in ELF 500 group than those in ELF-100 and sham groups ($p < 0.05$). MDA, TOS, and OSI values were found to be higher in ELF-500 group than those in ELF-100 and sham groups ($p < 0.05$). In conclusion, apoptosis was not changed by long-term ELF-MF exposure, while both 100 and 500 µT ELF-MF exposure induced toxic effect in the rat brain by increasing oxidative stress and diminishing antioxidant defense system.

(F) (OX) (MA) **(E) Akdag MZ, Dasdag S, Cakir DU, Yokus B, Kizil G, Kizil M. Do 100- and 500-µT ELF magnetic fields alter beta-amyloid protein, protein carbonyl and malondialdehyde in rat brains? Electromagn Biol Med. 32(3):363-372, 2013. (AS, CE, CC, OX)**

Several studies still state that presently accepted safety standards for extremely low-frequency magnetic fields (ELF-MFs) do not provide adequate protection, and therefore the standards are still open to question. To help resolve this question, the aim of this study was to illuminate the interaction between biomolecules and ELF-MFs by investigating the effect of ELF-MFs on beta-amyloid protein (BAP), protein carbonyl (PC) and malondialdehyde (MDA) in rat brain. For this study, 30 adult male Sprague-Dawley rats were used, which were divided into two experimental groups and a sham exposed group. Rats in two experimental groups were exposed to 100- and 500-µT ELF-MFs (50 Hz) for 2 h/day for 10 months, which are the generally accepted safety standards for public and occupational exposures. The same procedures were applied to the rats in the sham group, but with the generator turned off. The results of this study showed that neither ELF-MFs used in this study altered BAP level significantly ($p>0.05$). However, PC and MDA levels were increased by the exposure to 100- and 500-µT ELF-MFs ($p < 0.0001$). In conclusion, both PC and MDA levels were altered by long-term exposure to either 100 or 500

µT ELF-MF. However, many further and more comprehensive studies will be required to elucidate the interaction mechanisms between ELF-MFs exposure and living organisms.

(F) (OX) **(E) Akpinar D, Ozturk N, Ozen S, Agar A, Yargicoglu P. The effect of different strengths of extremely low-frequency electric fields on antioxidant status, lipid peroxidation, and visual evoked potentials. Electromagn Biol Med. 31(4):436-448, 2012. (AS, CE, OX, EE)**

The aim of the study was to investigate the effects of extremely low-frequency electric field (ELF EF) on visual evoked potential (VEP), thiobarbituric acid reactive substances (TBARS), total antioxidant status (TAS), total oxidant status (TOS), and oxidant stress index (OSI). Thirty female Wistar rats, aged 3 months, were divided into three equal groups: Control (C), the group exposed to EF at 12 kV/m strength (E12), and the group exposed to EF at 18 kV/m strength (E18). Electric field was applied to the E12 and E18 groups for 14 days (1 h/day). Brain and retina TBARS, TOS, and OSI were significantly increased in the E12 and E18 groups with respect to the control group. Also, TBARS levels were significantly increased in the E18 group compared with the E12 group. Electric fields significantly decreased TAS levels in both brain and retina in E12 and E18 groups with respect to the control group. All VEP components were significantly prolonged in rats exposed to electric fields compared to control group. In addition, all latencies of VEP components were increased in the E18 group with respect to the E12 group. It is conceivable to suggest that EF-induced lipid peroxidation may play an important role in changes of VEP parameters.

(E) Albert L, Olivier F, Jolivet A, Chauvaud L, Chauvaud S. Insights into the behavioural responses of juvenile thornback ray Raja clavata to alternating and direct current magnetic fields. J Fish Biol 100(3):645-659, 2022. (AS, AE, BE)

As part of energy transition, marine renewable energy devices (MRED) are currently expanding in developed countries inducing the deployment of dense networks of submarine power cables. Concern has thus raised about the cable magnetic emissions (direct or alternating current) because of potential interference with the sensorial environment of magneto-sensitive species, such as sharks and rays. This study sought to assess the short-term behavioural responses of juvenile thornback rays (Raja clavata) (n = 15) to direct and alternating (50 Hz) uniform 450-µT artificial magnetic fields using 1 h focal-sampling design based on a detailed ethogram. Careful control of magnetic fields' temporal and spatial scales was obtained in laboratory conditions through a custom-made Helmholtz coil device. Overall, qualitative or quantitative behavioural responses of juvenile rays did not significantly vary between control vs. exposed individuals over the morning period. Nonetheless, rays under direct current magnetic field increased their activity over the midday period. Synchronisation patterns were also observed for individuals receiving alternating current exposure (chronologic and qualitative similarities) coupled with a high inter-individual variance. Further studies should consider larger batches of juveniles to address the effect of long-term exposure and explore the sensitivity range of rays with dose-response designs.

(F) **(NE) Aldinucci C, Carretta A, Maiorca SM, Leoncini S, Signorini C, Ciccoli L, Pessina GP. Effects of 50 Hz electromagnetic fields on rat cortical synaptosomes. Toxicol Ind Health. 25(4-5):249-252, 2009. (CS, CC, AE)**

Nerve cells are very responsive to weak pulsed electromagnetic fields (EMFs). Such non-ionizing radiation, with frequencies of 0-300 Hz and 0.1-100 mT, can affect several cellular activities, with unusual dose-response characteristics. The present study examined the effect of a 2-h exposure of synaptosomes on a system generating a peak magnetic field of 2 mT. We evaluated the changes of the synaptosomal mitochondrial respiration rate and ATP production, membrane potential, intrasynaptosomal Ca2+ concentration, and the release of free iron and F2-isoprostanes. O2 consumption and ATP production remained unchanged in exposed synaptosomes. The intrasynaptosomal Ca2+ concentration decreased slowly and no depolarization of the synaptosomal membrane was detected. Finally, the release of free iron and F2-isoprostanes by synaptosomal suspensions also remained unchanged after EMF exposure. These results indicate that the physiological behavior of cortical synaptosomes was unaffected by weak pulsed EMFs.

(E) Aliyari H, Hedayat Sahraei, Sahar Golabi, Mohammad Bagher Menhaj, Masoomeh Kazemi, Seyed Hossein Hosseinian. The Effect of Electrical Fields From High-voltage Transmission Line on Cognitive, Biological, and Anatomical Changes in Male Rhesus macaque Monkeys Using MRI: A Case Report Study. Basic Clin Neurosci 13(4):433-442, 2022. (AS, CE, MC, BE)

Introduction: Living near high-voltage power lines and exposure to high-frequency electromagnetic fields (EMFs) is a potentially serious hazard to animal and human health. The present study was conducted to evaluate the effect of high-frequency EMFs from simulated high-voltage electric towers on cognitive, anatomical, and biological changes in the male macaque. **Methods:** In this study, two Rhesus macaque were recruited, one experimental and one control. The experimental subject was exposed to EMFs from 3 kV/m simulated electric towers with a specific protocol and the control subject was tested without irradiation (4h per day, for 30 days). All required tests were performed before and after the intervention on experimental and control monkeys. The anatomical alternation of the prefrontal area (PFA) was measured by MRI images. All tests were performed on irradiated and control animals before and after the intervention and the results were compared between irradiated and control animals. **Results:** The results of the present study indicated increased white blood cell counts after high-frequency EMFs irradiation. Also, the red blood cell counts showed a decreasing trend after irradiation. The plasma adrenaline level increased after irradiation. Besides, the blood glucose levels increased after irradiation. The PFA was different before and after the irradiation. Moreover, some behavioral disorders, such as fatigue, drowsiness, anorexia, and insomnia were observed after irradiation. **Conclusion:** The results of biological tests and MRI showed an elevated risk of immunodeficiency disorders, weakness, and behavioral disorders. People who live or work near high-voltage electric towers with high-frequency EMFs are warned. **Highlights:** Magnetic, and electric fields from high pressure towers caused negative effects in terms of biology and even anatomical changes in the prefrontal part of the brain. Disturbance in the prefrontal part of the

brain caused the monkey's cognitive and behavioral disorder.An increase in white blood cells, a decrease in red blood cells, and an increase in the adrenaline and blood sugar were indicative of biological disorders after wave exposure in male rhesus monkeys.The effects of magnetic and electric fields resulting from high pressure towers on the nerves and psyche require health researchers to do more studies.

(B) **(E) Alizadeh MAM, Abrari K, Blouki TL, Ghorbanian MT, Jadidi M. Pulsed electromagnetic field attenuated PTSD-induced failure of conditioned fear extinction. Iran J Basic Med Sci 22(6):650-659, 2019. (AS, CE, BE, MA)**

Objectives: This study aimed to determine whether exposure to pulsed electromagnetic field (PEMF) can impair behavioral failure as induced by PTSD, and also its possible effects on hippocampal neurogenesis. PEMF was used as a non-invasive therapeutic tool in psychiatry. **Materials and methods:** Male rats were divided into Control-Sham exposed, Control-PEMF, PTSD-Sham exposed, and PTSD-PEMF groups. PTSD rats were conducted by the single prolonged stress procedures and then conditioned by the contextual fear conditioning apparatus. Control rats were only conditioned. Experimental rats were submitted to daily PEMF (7 mT, 30 Hz for 16 min/day, 14 days). Sham-exposed groups were submitted to the turned off PEMF apparatus. Fear extinction, sensitized fear and anxiety, cell density in the hippocampus, and proliferation and survival rate of BrdU-labeled cells were evaluated. **Results:** Freezing of PTSD-PEMF rats was significantly lower than PTSD-Sham exposed. In the PTSD-PEMF, center and total crossing in open field, also the percentage of open arms entry and time in the elevated plus maze, significantly increased as compared with PTSD-Sham exposed ($P<0.001$). Numbers of CA1, CA3, and DG cells in PTSD-PEMF and Control-Sham exposed groups were significantly more than PTSD-Sham exposed ($P<0.001$). There were more BrdU-positive cells in the DG of the PTSD-PEMF as compared with the PTSD-Sham exposed. Qualitative observations showed an increased number of surviving BrdU-positive cells in the PTSD-PEMF as compared with PTSD-Sham exposed. **Conclusion:** Using 14-day PEM attenuates the PTSD-induced failure of conditioned fear extinction and exaggerated sensitized fear, and this might be related to the neuroprotective effects of magnetic fields on the hippocampus.

(B) **(E) Alsaeed I, Al-Somali F, Sakhnini L, Aljarallah OS, Hamdan RM, Bubishate SA, Sarfaraz ZK, Kamal A. Autism-relevant social abnormalities in mice exposed perinatally to extremely low frequency electromagnetic fields. Int J Dev Neurosci. 37:58-64, 2014. (AS, CE, BE, DE)**

The incidence of autism spectrum disorders (ASD) has been rising, but the causes of ASD remain largely unidentified. Collective data have implicated the increased human exposure to electromagnetic fields (EMF) in the increasing incidence of ASD. There are established biological effects of extremely low-frequency (ELF) EMF, but the relation to ASD is not investigated enough. In this study we examined the effects of perinatal exposure to ELF EMF on some ASD-relevant behavioral parameters in mice. The EMF was delivered via a Helmholtz coil pair. Male BALB/C mice were used and divided into exposed and control groups (n=8 and n=9, respectively). Tests were used to assess sociability, preference for social novelty, locomotion, anxiety, exploratory behavior, motor coordination, and olfaction. The examined mice were all males and exposed to EMF during the last week of gestation and for 7 days after delivery. The

exposed mice demonstrated a lack of normal sociability and preference for social novelty while maintaining normal anxiety-like behavior, locomotion, motor coordination, and olfaction. Exposed mice also demonstrated decreased exploratory activity. We concluded that these results are supportive of the hypothesis of a causal link between exposure to ELF-EMF and ASD; however, replications of the study with further tests are recommended.

(F) (E) **Amara S, Douki T, Garel C, Favier A, Sakly M, Rhouma KB, Abdelmelek H. Effects of static magnetic field exposure on antioxidative enzymes activity and DNA in rat brain. Gen Physiol Biophys. 28(3):260-265, 2009. (AS, CE, OX)**

The present study was undertaken in order to investigate the effects of static magnetic field (SMF) exposure on the antioxidative enzymes activity, malondialdehyde (MDA) concentration and DNA oxidation in male rat brain. The exposure of rats to SMF (128 mT, 1 h/day during 30 consecutive days) decreased the glutathione peroxidase (GPx; -39%, $p < 0.05$), CuZn superoxide dismutase (CuZn-SOD; -35%, $p < 0.05$) and catalase (-59%, $p < 0.05$) activities in frontal cortex. The same treatment decreased the CuZn-SOD (-51%, $p < 0.05$) and Mn-SOD (-13%, $p < 0.05$) activities in hippocampus. However, the glutathione levels remained unchanged in the both brain structures. In the hippocampus, SMF exposure increased MDA concentration (+32%, $p < 0.05$). Interestingly, exposed-rats to SMF displayed a significant increase of metallothioneins level in frontal cortex (+100%, $p < 0.05$), while the 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodGuo) concentration remained unaffected, indicating the absence of DNA oxidation. Our results indicated that sub-chronic exposure to SMF induced oxidative stress in rat hippocampus and frontal cortex. Metallothionein induction protected probably DNA against oxidative damage.

(F, OX) (E) **Amara S, Douki T, Garrel C, Favier A, Ben Rhouma K, Sakly M, Abdelmelek H.**
Effects of static magnetic field and cadmium on oxidative stress and DNA damage in rat cortex brain and hippocampus. Toxicol Ind Health. 27(2):99-106, 2011. (AS, CE, OX)

The present study was undertaken to determine the effect of co-exposure to static magnetic field (SMF) and cadmium (Cd) on the antioxidant enzymes activity and DNA integrity in rat brain. Sub-chronic exposure to CdCl (CdCl(2), 40 mg/L, per os) for 30 days resulted in a significant reduction in antioxidant enzyme activity such as the glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD) in frontal cortex and hippocampus. Total GSH were decreased in the frontal cortex of the Cd-exposed group. Cd exposure induced an increase in malondialdehyde (MDA) concentration in the frontal cortex and hippocampus. Moreover, the same exposure increased 8-oxo-7,8-dihydro-2-desoxyguanosine (8-oxodGuo) level in rat brain. Interestingly, the combined effect of SMF (128 mT, 1 hour/day for 30 consecutive days) and CdCl (40 mg/L, per os) decreased the SOD activity and glutathione level in frontal cortex as compared with the Cd group. Moreover, the association between SMF and Cd increased MDA concentration in frontal cortex as compared with Cd-exposed rats. DNA

analysis revealed that SMF exposure failed to alter 8-oxodGuo concentration in Cd-exposed rats. Our data showed that Cd exposure altered the antioxidant enzymes activity and induced oxidative DNA lesions in rat brain. The combined effect of SMF and Cd increased oxidative damage in rat brain as compared with Cd-exposed rats.

(B, MA) (E) Ambalayam S, Jain S, Mathur R. Abnormal feeding behaviour in spinalised rats is mediated by hypothalamus: Restorative effect of exposure to extremely low frequency magnetic field. Spinal Cord. 54:1076-1087, 2016. (AS, CE, BE, MA)

STUDY DESIGN: Experimental study. OBJECTIVES: To investigate the role of hypothalamus in abnormal feeding behaviour after spinal cord injury (SCI) and the effect of exposure to extremely low frequency magnetic field (ELF-MF) on it. SETTING: India. METHODS: Male Wistar rats (n=44) were divided into Sham (laminectomy), SCI (complete transection of T13 spinal cord), SCI+MF (ELF-MF exposure to SCI rats), VMHL (lesion of ventromedial hypothalamus; VMH), SCI+VMHL (VMHL after SCI) and SCI+VMHL+MF (ELF-MF exposure to SCI+VMHL rats) groups. Food intake (FI), water intake (WI), calorie intake (CI), body weight (BWT), taste preference and sucrose-induced biphasic (SIB) response to noxious stimulus were studied pre and post surgery. Neuronal activity at VMH was assessed by c-Fos immunohistochemistry. The extent of neuronal degeneration and regeneration in spinal cord was assessed microscopically. RESULTS: Data revealed post-SCI decrease in FI, WI, CI and BWT, preference for sodium chloride and citric acid, prolonged analgesic phase of SIB and increased c-Fos immunoreactivity in VMH of SCI rats vs Sham rats. VMH lesion increased FI, WI, CI, BW, preference for sweet tastants and abolished SIB, whereas in SCI+VMHL rats it abolished the effects of SCI on these parameters indicating probable involvement of VMH in SCI-induced alteration in feeding behaviour. Exposure to MF improved the study parameters in SCI rats and reduced the c-Fos immunoreactivity in VMH besides reduction in lesion volume, greater myelination and neuronal regeneration at SCI site. CONCLUSION: SCI influences VMH, leading to alteration in feeding behaviour, which is improved by exposure to ELF-MF.

Ambron R. Synaptic sensitization in the anterior cingulate cortex sustains the consciousness of pain via synchronized oscillating electromagnetic waves. Front Hum Neurosci 18:1462211, 2024. (opinion)

A recent report showed that experiencing pain requires not only activities in the brain, but also the generation of electric fields in a defined area of the anterior cingulate cortex (ACC). The present manuscript presents evidence that electromagnetic (EM) waves are also necessary. Action potentials (APs) encoding information about an injury stimulate thousands synapses on pyramidal neurons within the ACC resulting in the generation of synchronized oscillating (EM) waves and the activation of NMDA receptors. The latter induces a long-term potentiation (LTP)

in the pyramidal dendrites that is necessary to experience both neuropathic and visceral pain. The LTP sensitizes transmission across the synapses that sustains the duration of the waves and the pain, EM waves containing information about the injury travel throughout the brain and studies using transcranial stimulation indicate that they can induce NMDA-mediated LTP in distant neuronal circuits. What is ultimately experienced as pain depends on the almost instantaneous integration of information from numerous neuronal centers, such as the amygdala, that are widely separated in the brain. These centers also generate EM waves and I propose that the EM waves from these centers interact to rapidly adjust the intensity of the pain to accommodate past and present circumstances. Where the waves are transformed into a consciousness of pain is unknown. One possibility is the mind which, according to contemporary theories, is where conscious experiences arise. The hypothesis can be tested directly by blocking the waves from the ACC. If correct, the waves would open new avenues of research into the relationship between the brain, consciousness, and the mind.

(F, MA) (E) Amirifalah Z, Firoozabadi SM, Shafiei SA. Local Exposure of Brain Central Areas to a Pulsed ELF Magnetic Field for a Purposeful Change in EEG. Clin EEG Neurosci. 44(1):44-52, 2013. (HU, EE)

This study examines the simultaneous exposure of 2 brain areas in the location of central electrodes (C3 and C4) to a weak and pulsed extremely low-frequency magnetic field (ELF-MF) on the electroencephalogram (EEG). The intent is to change the EEG for a therapeutic application, such as neurofeedback, by inducing the "resonance effect." A total of 10 healthy women received 9 minutes of ELF-MF (intensity 200 µT) and sham in a counterbalanced design. ELF-MF exposure frequencies were 10, 14, and 18 Hz. The paired t test revealed that local pulsed ELF-MF significantly decreases beta (15-25 Hz), sensorimotor rhythm (13-15 Hz), and theta (4-8 Hz) powers at a frequency of 10 Hz in C3 and C4 regions (12.0%-26.6%) after exposure, in comparison with that achieved during the exposure ($P < .05$). Variations during the exposure were transient and different from those after. The resonance effect was observed nowhere around the regions. The study suggests that this technique may be applied in the treatment of anxiety; however, further investigation is needed.

(E) Ammari M, Jeljeli M, Maaroufi K, Roy V, Sakly M, Hafedh Abdelmelek H. Static magnetic field exposure affects behavior and learning in rats. Electromagn Biol Med 27(2):185-196, 2008.(AS, CE, BE)

The present work investigated the behavioral effects of a moderate exposure (1 h per day for 5 consecutive days) to a static magnetic field (SMF, 128 mT) in male rats. SMF effects were evaluated in two sets of control and SMF-exposed rats. One set of animals was used for evaluation of SMF potential effects on emotional behaviors in the elevated plus maze and in the open field. The other set of animals was tested for learning and memory abilities in different procedures of the Morris water maze task. We found no significant difference between control and SMF-exposed rats in anxiety tests. However, the ratio of open arms time in the plus maze was reduced by half in SMF-exposed rats. In the Morris water maze, SMF-exposed rats were partially impaired during the initial learning task as well as in the retention task at one week. We

conclude that static magnetic field exposure altered emotional behaviors in the plus maze and led to cognitive impairments, or at least to substantial attention disorders, in the Morris water maze.

(B) (NE) Andrianome S, Hugueville L, de Seze R, Hanot-Roy M, Blazy K, Gamez C, Selmaoui B. Disturbed sleep in individuals with Idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF): Melatonin assessment as a biological marker. Bioelectromagnetics. 37:175-182, 2016. (HU, CC)

Individuals who suffer from idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) complain of a variety of adverse health effects. Troubled sleep remains a recurrent and common symptom in IEI-EMF individuals. Melatonin, a circadian hormone, plays a major role in the sleep process. In this study, we compared levels of melatonin between a sensitive group (IEI-EMF, $n = 30$) and a non-sensitive control group (non IEI-EMF, $n = 25$) without exposure to electromagnetic sources. Three questionnaires were used to evaluate the subjective quality and sleep quantity: the Epworth Sleepiness Scale, the Pittsburgh Sleep Quality Index and the Spiegel Sleep Inventory. Melatonin was quantified in saliva and its major metabolite 6-sulfatoxymelatonin (aMT6s) in urine. Melatonin levels were compared by a two-way analysis of variance at various times between the control and IEI-EMF group. Despite significantly different sleep scores between the two groups, with a lower score in the IEI-EMF group ($P < 0.001$), no statistical difference was found between the two groups for saliva melatonin ($P > 0.05$) and urine aMT6s ($P > 0.05$).

(F, B, MA, OX) (E) Ansari AM, Farzampour S, Sadr A, Shekarchi B, Majidzadeh-A K. Effects of short term and long term extremely low frequency magnetic field on depressive disorder in mice: Involvement of nitric oxide pathway. Life Sci. 146:52-57, 2016. (AS, AE, CE, BE, OX)

AIMS: Previous reports on the possible effects of Extremely Low Frequency Magnetic Fields (ELF MF) on mood have been paradoxical in different settings while no study has yet been conducted on animal behavior. In addition, it was shown that ELF MF exposure makes an increase in brain nitric oxide level. Therefore, in the current study, we aimed to assess the possible effect(s) of ELF MF exposure on mice Forced Swimming Test (FST) and evaluate the probable role of the increased level of nitric oxide in the observed behavior. MAIN METHODS: Male adult mice NMRI were recruited to investigate the short term and long term ELF MF exposure (0.5 mT and 50Hz, single 2h and 2weeks 2h a day). Loco motor behavior was assessed by using Open-Field Test (OFT) followed by FST to evaluate the immobility time. Accordingly, NΩ-nitro-L-arginine methyl ester 30mg/kg was used to exert anti-depressant like effect. KEY FINDINGS: According to the results, short term exposure did not alter the immobility time, whereas long term exposure significantly reduces immobility time ($p<0.01$). However, it was revealed that the locomotion did not differ among all experimental groups. Short term exposure reversed the anti-depressant like effect resulting from 30mg/kg of NΩ-nitro-L-arginine methyl ester ($p<0.01$). SIGNIFICANCE: It has been concluded that long term exposure could alter the depressive disorder in mice, whereas short term exposure has no significant effect. Also, reversing the anti-depressant activity of L-NAME indicates a probable increase in the brain nitric oxide.

(B) (E) Ayoobi F, Shamsizadeh A, Shafiei SA. The effect of local extremely low frequency magnetic field on student sleepiness. Neurol Res. 39:1080-1085, 2017. (HU, AE, BE)

Objectives: Lack of high-quality sleep causes serious side effects. The current study aimed to investigate the impact of local extremely low frequency magnetic field (ELF-MF) on sleep and drowsiness in healthy young adults. Methods: Sixty-five young adults (32 males and 31 females, aged 18-24, participated voluntarily in this randomized crossover clinical trial. 200 microTesla MF (3 minutes duration) at three frequencies (10, 14 and 18 Hz) was applied to the skull in areas C3, Cz and C4, respectively. The Stanford Sleepiness Scale (SSS) or Consciousness Test (CT), Epworth Sleepiness Scale (ESS) and Peabody Picture Vocabulary Test were used to evaluate drowsiness, sleepiness, and reaction time. These tests were done both before and after application of ELF-MF or sham operation. Results: Minimum reaction time after exposure to ELF-MF increased compared to that before exposure ($P = 0.03$), while it was not significant for the sham group ($P = 0.63$). From the ESS questionnaire, the results indicated that there was no significant difference for males or females between the exposure and sham groups. The mean of the SSS scores was no different compared to that before exposure. Conclusion: The results of this study demonstrated that exposure to ELF-MF may influence reaction time in young healthy people. However, as the results of ESS and SSS were not different between exposure and non-exposure groups, further studies using larger sample sizes are recommended in order to reach better interpretations of the effects of ELF-MF on sleepiness in young people.

(F) (NE) Azanza MJ, del Moral A, Calvo AC, Pérez-Bruzón RN, Junquera C. Synchronization dynamics induced on pairs of neurons under applied weak alternating magnetic fields. Comp Biochem Physiol A Mol Integr Physiol. 166(4):603-618, 2013.(CS, AE, EE, MC)

Pairs of Helix aspersa neurons show an alternating magnetic field dependent frequency synchronization (AMFS) when exposed to a weak (amplitude B0 between 0.2 and 150 Gauss (G)) alternating magnetic field (AMF) of extremely low frequency (ELF, fM = 50 Hz). We have compared the AMFS patterns of discharge with: i) the synaptic activity promoted by glutamate and acetylcholine; ii) the activity induced by caffeine; iii) the bioelectric activity induced on neurons interconnected by electric synapses. AMFS activity reveals several specific features: i) a tight coincidence in time of the pattern and frequency, f, of discharge; ii) it is induced in the time interval of field application; iii) it is dependent on the intensity of the sinusoidal applied magnetic field; iv) elicited biphasic responses (excitation followed by inhibition) run in parallel for the pair of neurons; and v) some neuron pairs either spontaneously or AMF synchronized can be desynchronized under applied higher AMF. Our electron microscopy studies reveal gap-like junctions confirming our immunocytochemistry results about expression of connexin 26 (Cx26) in 4.7% of Helix neurons. AMF and carbenoxolone did not induce any significant effect on spontaneous synchronization through electric synapses.

(E) Azizi E, Fatemeh Ayoobi, Ali Shamsizadeh, Amir Moghadam-Ahmadi, Seyed Ali Shafiei, Alireza Khoshdel, Mohammad Reza Mirzaei. Effect of Short-time Exposure of Local Extremely Low-Frequency Magnetic Fields on Sleepiness in Male Rats. Basic Clin Neurosci 13(4):519-529, 2022. (AS, CE, CC, BE)

Introduction: Lack of high-quality sleep causes severe side effects like anxiety and changes in plasma concentration of oxalate. The current study investigated the impact of local extremely low-frequency magnetic fields (ELF-MFs) on inducing sleep (sleepiness) and anxiety in male rats. **Methods:** In this experimental study, 40 male rats were divided into four groups (n=10 for each group). The ELF-MF exposure (0, 10, and 18 Hz) was applied with an intensity of 200µT for three days (10 min/d). The sham-treated animal did not receive ELF-MF. Serum levels of oxalic acid (OA) and sleepiness were measured before and after the last exposure to ELF-MF or sham. Anxiety, sleepiness, and OA were measured using the elevated plus maze, open-field test (OFT), and ELISA test. **Results:** A comparison of oxalate levels before and after exposure to ELF-MF revealed that ELF-MF (10 Hz) decreased the serum level of oxalate ($P<0.05$). Comparing open/closed arm entry (in an elevated plus maze) between before and after exposure to ELFMF revealed significant differences. Also, frequency, velocity, and distance moved were decreased in the open-field test. **Conclusion:** Results of the present study demonstrated that ELF-MF with short-time exposure may modulate the metabolism of OA and may modulate anxiety-like behavior or kind of induction of sleepiness in male rats. **Highlights:** Oxalate acid concentration may reduce after short time ELF-MF exposure. Locomotor activity in male rats may decrease after the ELF-MF exposure. Short time ELF-MF exposure may induce sleepiness in male rats that may be used to treat sleep disorders.

(E) Baaken D, Dechent D, Blettner M, Drießen S, Merzenich H. Occupational Exposure to Extremely Low-Frequency Magnetic Fields and Risk of Amyotrophic Lateral Sclerosis: Results of a Feasibility Study for a Pooled Analysis of Original Data. Bioelectromagnetics 42:271-283, 2021.(ND)

Previous meta-analyses have suggested an increased risk of amyotrophic lateral sclerosis (ALS) associated with occupational exposure to extremely low-frequency magnetic fields (ELF-MF). However, results should be interpreted with caution since studies were methodologically heterogeneous. Here, we assessed the feasibility of a pooling study to harmonize and re-analyze available original data. A systematic literature search was conducted. Published epidemiological studies were identified in PubMed and EMF-Portal from literature databases' inception dates until January 2019. The characteristics of all studies were described, including exposure metrics, exposure categories, and confounders. A survey among the principal investigators (PI) was carried out to assess their willingness to provide their original data. The statistical power of a pooling study was evaluated. We identified 15 articles published between 1997 and 2019. Studies differed in terms of outcome, study population, exposure assessment, and exposure metrics. Most studies assessed ELF-MF as average magnetic flux density per working day; however, exposure categories varied widely. The pattern of adjustment for confounders was heterogeneous between studies, with age, sex, and socioeconomic status being most frequent. Eight PI expressed their willingness to provide original data. A relative risk of ≥1.14 for ALS and occupational exposure to ELF-MF can be detected with a power of more than 80% in a pooled study. The pooling of original data is recommended and could contribute to a better understanding of ELF-MF in the etiology of ALS based on a large database and reduced heterogeneity due to a standardized analysis protocol with harmonized exposure metrics and exposure categories.

(E) Bademoğlu G, Erdal N, Uzun C, Taşdelen B The effects of pulsed electromagnetic field on experimentally induced sciatic nerve injury in rats. Electromagn Biol Med 40(3):408-419, 2021.(AS, CE,BE, MA)

Some experimental research indicates that low-frequency pulsed electromagnetic field (PEMF) stimulation may accelerate regeneration in sciatic nerve injury. However, little research has examined the electrophysiological and functional properties of regenerating peripheral nerves under PEMF. The main aim of the present study is to investigate the effects of PEMF on sciatic nerve regeneration in short- and long-term processes with electrophysiologically and functionally after crushing damage. Crush lesions were performed using jewelery forceps for 30 s. After crush injury of the sciatic nerves, 24 female Wistar-Albino rats were divided into 3 groups with 8 rats in each group: SH(Sham), SNI (Sciatic Nerve Injury), SNI+PEMF(Sciatic Nerve Injury+Pulsed Electromagnetic Field). SNI+PEMF group was exposed to PEMF (4 h/day, intensity; 0.3mT, low-frequency; 2 Hz) for 40-days. Electrophysiological records (at the beginning and 1st, 2nd, 4th and 6th weeks post-crush) and functional footprints (at 1st, 2nd, 3rd, 4th, 5th and 6th weeks post crush) were measured from all groups during the experiment. The results were compared to SNI and SNI+PEMF groups, it was found that amplitude and area parameters in the first-week were significantly higher and latency was lower in the SNI+PEMF group than in the SNI group ($p < 0,05$). However, the effect of PEMF was not significant in the 2nd, 4th, 6th weeks. In addition, in the 1st and 2nd weeks, the SSI parameters were significantly

higher in SNI+PMF group than SNI group ($p < .05$). These results indicate that low-frequency PEMF is not effective for long-periods of application time while PEMF may be useful during the short-term recovery period.

(F, MA) (E) Bai WF, Xu WC, Feng Y, Huang H, Li XP, Deng CY, Zhang MS. Fifty-Hertz electromagnetic fields facilitate the induction of rat bone mesenchymal stromal cells to differentiate into functional neurons. Cytotherapy. 15(8):961-970, 2013. (CS, CE, MC, MA, ND)

BACKGROUND AIMS: Research results have shown that bone mesenchymal stromal cells (BMSC) can different into neural cells. Electromagnetic fields (EMF) play a role in regulating cell proliferation and differentiation, but the mechanisms behind this are unknown. In the present study, we explored the efficacy of EMF on the induction of rat BMSC differentiation into neurons in vitro. METHODS: First, rat BMSC were induced in a nerve cell culture environment and divided into three groups: an EMF induction treatment group (frequency of 50 Hz, magnetic induction of 5 mT, 60 min per day for 12 days), an induction-only group and a control group. Second, we observed cell phenotypes in a confocal microscope, tested gene expression through the use of reverse transcriptase-polymerase chain reaction, and detected postsynaptic currents by means of a cell patch-clamp. We analyzed the cell cycles and the portion of cells expressing neural cell markers with the use of flow cytometry. RESULTS: The results indicated that EMF can facilitate BMSC differentiation into neural cells, which expressed neuronal-specific markers and genes; they formed synaptic junctions and pulsed excitatory postsynaptic currents. At the same time, the G0-G1 phase ratio recorded by means of flow cytometry gradually decreased under the EMF treatment, whereas there was an increase of S-phase ratio, and the portion of cells expressing neuronal-specific markers increased. CONCLUSIONS: Given that a noninvasive treatment of 50-Hz EMF could significantly facilitate BMSC to differentiate into functional neurons, EMF appears to be a promising clinical option for stem cell transplantation therapies to combat central nervous system diseases.

(F, MA) (E) Bai W, Li M, Xu W, Zhang M. Comparison of effects of high- and low-frequency electromagnetic fields on proliferation and differentiation of neural stem cells. Neurosci Lett 741:135463, 2021. (CS, CE, MC, MA)

To compare the effects of high- (HF-EMF) and low-frequency electromagnetic fields (LF-EMF) on the proliferation and differentiation of neural stem cells (NSCs). NSCs were obtained from SD rat hippocampus and cultured in suspension and adherent differentiation media. NSCs were exposed to LF-EMF (5 m T, 50 Hz, 30 min daily), HF-EMF (maximum magnetic induction 2.5 T, 40% MO, 50 Hz, 10 min daily) and no electromagnetic field. At 3 d, cell viability and quantity of NSCs in suspension were detected by CCK-8 assay and cell counting plate. Immunofluorescence staining and qRT-PCR were performed to detect the percentage of Tuj-1 and GFAP-positive NSCs and the expression of Tuj-1 and GFAP mRNA. The P3 NSCs were positive with Nestin and induced NSCs expressed Tuj-1, GFAP and oligodendrocyte markers (MBP). CCK-8 assay and cell counting showed that the OD value and quantity of LF-EMF group were significantly higher than those in other two groups (both $P < 0.05$). Compared with

the control group, the OD value and quantity were significantly higher in the HF-EMF group ($P < 0.05$). Immunofluorescence staining and qRT-PCR revealed that the percentage of Tuj-1 positive cells and the expression of Tuj-1 mRNA of NSCs exposed to LF-EMF were the highest (both $P < 0.05$). The proportion of GFAP-positive NSCs and the expression of GFAP mRNA did not significantly differ among three groups (all $P > 0.05$). Both 50 Hz LF-EMF and HF-EMF can promote the proliferation of NSCs in vitro and LF-EMF can accelerate NSCs to differentiate into neurons.

(B) (E) Balassa T, Szemerszky R, Bárdos G. Effect of short-term 50 Hz electromagnetic field exposure on the behavior of rats. Acta Physiol Hung. 96(4):437-448, 2009. (AS, BE, AE)

Extremely low-frequency electromagnetic field generated by transformer stations located within buildings has been suspected to initiate non-specific health problems. This possibility was examined in model experiments in rats. Following short-term exposure (50 Hz, 500 mircoT, 20 min), situational and social anxiety as well as locomotor activity pattern were examined by several different tests (elevated plus-maze, novel object exploration, social interaction and territoriality).Based on our results having obtained so far, it seems that these field parameters (that equals the official reference limit for workers) may cause some kind of discomfort, may influence behavior, increase passivity and situational anxiety, but has no verified effect on the social and territorial behavior.

(F) (E) Balassa T, Varró P, Elek S, Drozdovszky O, Szemerszky R, Világi I, Bárdos G. Changes in synaptic efficacy in rat brain slices following extremely low-frequency magnetic field exposure at embryonic and early postnatal age. Int J Dev Neurosci. 31(8):724-730, 2013. (AS, CE, EE, DE)

An earlier study demonstrated changes in synaptic efficacy and seizure susceptibility in adult rat brain slices following extremely low-frequency magnetic field (ELF-MF) exposure. The developing embryonic and early postnatal brain may be even more sensitive to MF exposure. The aim of the present study was to determine the effects of a long-term ELF-MF (0.5 and 3 mT, 50 Hz) exposure on synaptic functions in the developing brain. Rats were treated with chronic exposure to MF during two critical periods of brain development, i.e. in utero during the second gestation week or as newborns for 7 days starting 3 days after birth, respectively. Excitability and plasticity of neocortical and hippocampal areas were tested on brain slices by analyzing extracellular evoked field potentials. We demonstrated that the basic excitability of hippocampal slices (measured as amplitude of population spikes) was increased by both types of treatment (fetal 0.5 mT, newborn 3 mT). Neocortical slices seemed to be responsive mostly to the newborn treatment, the amplitude of excitatory postsynaptic potentials was increased. Fetal ELF-MF exposure significantly inhibited the paired-pulse depression (PPD) and there was a significant decrease in the efficacy of LTP (long-term potentiation induction) in neocortex, but not in hippocampus. On the other hand, neonatal treatment had no significant effect on plasticity phenomena. Results demonstrated that ELF-MF has significant effects on basic neuronal functions and synaptic plasticity in brain slice preparations originating from rats exposed either in fetal or in newborn period.

(E) Barassi G, Pokorski M, Pellegrino R, Supplizi M, Prosperi L, Marinucci C, Di Simone E, Mariani C, Younes A, Di Iorio A. Quantum Medicine: A Role of Extremely Low-Frequency Magnetic Fields in the Management of Chronic Pain. Adv Exp Med Biol 1375:23-28, 2022. (HU, CE, FC, MA)

Extremely low-frequency electromagnetic field (ELF-MF) therapy is a promising treatment for chronic pain, given its ability to interact with body homeostasis using water-mediated transmission mechanisms typical of quantum medicine. The present study aims to assess the effects of ELF-MF therapy on chronic pain in 49 patients suffering from various musculoskeletal disorders. The therapy was applied through a Quec Phisis setup generating the electromagnetic field as the ion cyclotronic resonance. Patients underwent eight therapy sessions of 45 min each performed every other day. The bioimpedance assessment was based on the comparison of the height-adjusted body resistance (R/h) and reactance (Xc/h) measured during the first and last sessions of eight-session treatment. Pain perception was quantified using the standard visual-analog scale. We found significant increases in both R/h and Xc/h parameters of body bioimpedance after electromagnetic therapy corresponding with reductions in pain perception. We conclude that the ELF-MF therapy can restore the body's state of health and thus seems a valid therapeutic approach for the treatment of musculoskeletal-derived pain.

(NE) Bassetto M, Reichl T, Kobylkov D, Kattnig DR, Winklhofer M, Hore PJ, Mouritsen H. No evidence for magnetic field effects on the behaviour of Drosophila. Nature. 620(7974):595-599, 2023. (AS, AE, BE)

Migratory songbirds have the remarkable ability to extract directional information from the Earth's magnetic field[1,2]. The exact mechanism of this light-dependent magnetic compass sense, however, is not fully understood. The most promising hypothesis focuses on the quantum spin dynamics of transient radical pairs formed in cryptochrome proteins in the retina[3-5]. Frustratingly, much of the supporting evidence for this theory is circumstantial, largely because of the extreme challenges posed by genetic modification of wild birds. Drosophila has therefore been recruited as a model organism, and several influential reports of cryptochrome-mediated magnetic field effects on fly behaviour have been widely interpreted as support for a radical pair-based mechanism in birds[6-23]. Here we report the results of an extensive study testing magnetic field effects on 97,658 flies moving in a two-arm maze and on 10,960 flies performing the spontaneous escape behaviour known as negative geotaxis. Under meticulously controlled conditions and with vast sample sizes, we have been unable to find evidence for magnetically sensitive behaviour in Drosophila. Moreover, after reassessment of the statistical approaches and sample sizes used in the studies that we tried to replicate, <u>we suggest that many-if not all-of the original results were false positives</u>. Our findings therefore cast considerable doubt on the existence of magnetic sensing in Drosophila and thus strongly suggest that night-migratory songbirds remain the organism of choice for elucidating the mechanism of light-dependent magnetoreception.

(F, MA) (E) Ben Yakir-Blumkin M, Loboda Y, Schächter L, Finberg JP. Neuroprotective effect of weak static magnetic fields in primary neuronal cultures. Neuroscience. 278:313-326, 2014. (CS, CE, CC, MA, ND)

Low intensity static magnetic fields (SMFs) interact with various biological tissues including the CNS, thereby affecting key biological processes such as gene expression, cell proliferation and differentiation, as well as apoptosis. Previous studies describing the effect of SMFs on apoptotic cell death in several non-neuronal cell lines, emphasize the importance of such a potential modulation in the case of neurodegenerative disorders, where apoptosis constitutes a major route via which neurons degenerate and die. In this study, we examine the effect of SMFs on neuronal survival in primary cortical and hippocampal neurons that constitute a suitable experimental system for modeling the neurodegenerative state in vitro. We show that weak SMF exposure interferes with the apoptotic programming in rat primary cortical and hippocampal neurons, thereby providing protection against etoposide-induced apoptosis in a dose- and time-dependent manner. Primary cortical neurons exposed to SMF (50 G) for 7 days exhibited a 57.1 ± 6.3% decrease in the percentage of cells undergoing apoptosis induced by etoposide (12 μM), accompanied by a marked decrease in the expression of the pro-apoptotic markers: cleaved poly ADP ribose polymerase-1, cleaved caspase-3, active caspase-9 and the phospho- histone H2A variant (Ser 139) by 41.0 ± 5.0%, 81.2 ± 5.0%, 72.9 ± 6.4%, 42.75 ± 2.9%, respectively, and by a 57.2 ± 1.0% decrease in the extent of mitochondrial membrane potential collapse. Using the L-type voltage-gated Ca^{2+} channel inhibitor nifedipine, which is selective to Ca^{2+} influx through $Ca_v1.2$, we found that the anti-apoptotic effect of SMFs was mediated by Ca^{2+} influx through these channels. Our findings demonstrating altered Ca^{2+}-influx in response to thapsigargin stimulation in SMF-exposed cortical neurons, along with enhanced inhibition of KCl-induced Ca^{2+}-influx through $Ca_v1.2$ channels and enhanced expression of $Ca_v1.2$ and $Ca_v1.3$ channels, allude to the involvement of voltage and store operated Ca^{2+} channels in various aspects of the protective effect exerted by SMFs. These findings show the potential susceptibility of the CNS to weak SMF exposure and have implications for the design of novel strategies for the treatment and/or prevention of neurodegenerative diseases.

(F, MA) (E) Benassi B, Filomeni G, Montagna C, Merla C, Lopresto V, Pinto R, Marino C, Consales C. Extremely Low Frequency Magnetic Field (ELF-MF) Exposure Sensitizes SH-SY5Y Cells to the Pro-Parkinson's Disease Toxin MPP. Mol Neurobiol. 53:4247-4260, 2016. (CS, OX, ND)

Parkinson's disease (PD) is a neurodegenerative disorder characterized by dopaminergic neuron loss, with an etiopathogenesis involving both genetic and environmental factors. The occupational/residential exposure to the electromagnetic fields has been recently associated with an increased risk of neurodegenerative diseases; it has been thus proposed that the extremely low frequency magnetic field (ELF-MF) may contribute to neurodegenerative etiopathogenesis, as its interaction with biological systems directly impairs redox homeostasis in specific areas of the brain. The molecular mechanisms elicited by ELF-MF, and their potential involvement in PD onset, still remain unclear. To this end, we set up a generator of ELF-MF able to stably and homogeneously reproduce environmental prolonged exposure to ELF-MF (50 Hz, 1 mT). Results obtained indicate that ELF-MF exposure alters cell response of SH-SY5Y cells to MPP^+. We demonstrate that ELF-MF does not affect per se survival, shape, and morphology of both proliferating and differentiated SH-SY5Y cells but significantly impairs redox homeostasis and thiol content, triggering an increase in protein carbonylation. As a result, toxicity of MPP^+,

even at low doses, is highly enhanced in ELF-MF-exposed cells due to a significant increase in ROS levels, potentiation of oxidative damage, and induction of a caspase-dependent apoptosis. Pre-incubation with the thiol antioxidants N-acetyl-L-cysteine and GSH ethyl-ester significantly reduces the extent of oxidative damage and protects cells from death induced by the combined treatment ELF-MF/MPP^+. Taken overall, our results demonstrate the redox-based molecular interaction between ELF-MF and PD neurotoxins in vitro, and open a new scenario for defining the synergy of environmental factors in PD onset.

(E) Bentwich J, Dobronevsky E, Aichenbaum S, Shorer R, Peretz R, Khaigrekht M, Marton RG, Rabey JM. Beneficial effect of repetitive transcranial magnetic stimulation combined with cognitive training for the treatment of Alzheimer's disease: a proof of concept study. J Neural Transm (Vienna). 118(3):463-471, 2011. (HU, CE, BE, FC, MA, ND)

The current drug treatment for Alzheimer's disease (AD) is only partially and temporary effective. Transcranial magnetic stimulation (TMS) is a non-invasive technique that generates an electric current inducing modulation in cortical excitability. In addition, cognitive training (COG) may improve cognitive functions in AD. Our aim was to treat AD patients combining high-frequency repetitive TMS interlaced with COG (rTMS-COG). Eight patients with probable AD, treated for more than 2 months with cholinesterase inhibitors, were subjected to daily rTMS-COG sessions (5/week) for 6 weeks, followed by maintenance sessions (2/week) for an additional 3 months. Six brain regions, located individually by MRI, were stimulated. COG tasks were developed to fit these regions. Primary objectives were average improvement of Alzheimer Disease Assessment Scale-Cognitive (ADAS-cog) and Clinical Global Impression of Change (CGIC) (after 6 weeks and 4.5 months, compared to baseline). Secondary objectives were average improvement of MMSE, ADAS-ADL, Hamilton Depression Scale (HAMILTON) and Neuropsychiatric Inventory (NPI). One patient abandoned the study after 2 months (severe urinary sepsis). ADAS-cog (average) improved by approximately 4 points after both 6 weeks and 4.5 months of treatment ($P < 0.01$ and $P < 0.05$) and CGIC by 1.0 and 1.6 points, respectively. MMSE, ADAS-ADL and HAMILTON improved, but without statistical significance. NPI did not change. No side effects were recorded. In this study, rTMS-COG (provided by Neuronix Ltd., Yokneam, Israel) seems a promising effective and safe modality for AD treatment, possibly as good as cholinesterase inhibitors. A European double blind study is underway.

Bertagna F, Lewis R, Silva SRP, McFadden J, Jeevaratnam K . Effects of electromagnetic fields on neuronal ion channels: a systematic review. Ann N Y Acad Sci 1499(1):82-103, 2021. (Review)

Many aspects of chemistry and biology are mediated by electromagnetic field (EMF) interactions. The central nervous system (CNS) is particularly sensitive to EMF stimuli. Studies have explored the direct effect of different EMFs on the electrical properties of neurons in the last two decades, particularly focusing on the role of voltage-gated ion channels (VGCs). This work aims to systematically review published evidence in the last two decades detailing the

effects of EMFs on neuronal ion channels as per the PRISM guidelines. Following a predetermined exclusion and inclusion criteria, 22 papers were included after searches on three online databases. Changes in calcium homeostasis, attributable to the voltage-gated calcium channels, were found to be the most commonly reported result of EMF exposure. EMF effects on the neuronal landscape appear to be diverse and greatly dependent on parameters, such as the field's frequency, exposure time, and intrinsic properties of the irradiated tissue, such as the expression of VGCs. Here, we systematically clarify how neuronal ion channels are particularly affected and differentially modulated by EMFs at multiple levels, such as gating dynamics, ion conductance, concentration in the membrane, and gene and protein expression. Ion channels represent a major transducer for EMF-related effects on the CNS.

(F, MA) (E) Bertolino G, Dutra Souza HC, de Araujo JE. Neuropathology and behavioral impairments in Wistar rats with a 6-OHDA lesion in the substantia nigra compacta and exposure to a static magnetic field. Electromagn Biol Med. 32(4):527-535, 2013. (AS, CE, BE, MC, ND, MA)

Studies have sought to assess various potential neuroprotective therapeutics in Parkinson's disease. The aim of this study was to evaluate the effects of static magnetic field stimulation 14 days after a 6-Hydroxydopamine (6-OHDA) substantia nigra compacta (SNc) lesion on motor behavior, as assessed by the rotarod (RR) test and brain tissue morphology. Forty male Wistar rats were used and were divided into five groups: control group, sham group (SG), lesion group (LG), lesion north pole group (LNPG) and lesion south pole group (LSPG). In groups with magnetic stimulation, a 3200-gauss magnet was fixed to the skull. After the experiments, the animals were anesthetized for brain perfusion. Coronal sections of the SNc were stained with Nissl. The RR test showed a decrease in the time spent on the apparatus in the LG compared with all groups. The LNPG and LSPG had significant increases in the time spent when compared to the LG. A morphometric analysis revealed a significant reduction in the number of neurons in the LG, LNPG and LSPG in relation to the SG. There were a higher number of neurons in the LNPG and LSPG than the LG, and a higher number of neurons in the LSPG than the LNPG. We observed that the LG, LNPG and LSPG showed a higher number of glial cells than the SG, and the LNPG and LSPG showed a lower number of glial cells than the LG. Our results demonstrate a potential therapeutic use of static magnetic fields for the preservation of motor behavior and brain morphology in the SNc after 14 days with 6-OHDA lesion.

(E) Bijlsma N, Conduit R, Kennedy G, Cohen M. Does radiofrequency radiation impact sleep? A double-blind, randomised, placebo-controlled, crossover pilot study. Front Public Health 12:1481537, 2024. (HU, CE, EE, BE)

The most common source of Radiofrequency Electromagnetic Field (RF-EMF) exposures during sleep includes digital devices, yet there are no studies investigating the impact of multi-night exposure to electromagnetic fields emitted from a baby monitor on sleep under real-world conditions in healthy adults. Given the rise in the number of people reporting to be sensitive to manmade electromagnetic fields, the ubiquitous use of Wi-Fi enabled digital devices and the lack of real-world data, we investigated the effect of 2.45 GHz radiofrequency exposure during sleep on subjective sleep quality, and objective sleep measures, heart rate variability and actigraphy in

healthy adults. This pilot study was a 4-week randomised, double-blind, crossover trial of 12 healthy adults. After a one-week run-in period, participants were randomised to exposure from either an active or inactive (sham) baby monitor for 7 nights and then crossed over to the alternate intervention after a one-week washout period. Subjective and objective assessments of sleep included the Pittsburgh Insomnia Rating Scale (PIRS-20), electroencephalography (EEG), actigraphy and heart rate variability (HRV) derived from electrocardiogram. Sleep quality was reduced significantly ($p < 0.05$) and clinically meaningful during RF-EMF exposure compared to sham-exposure as indicated by the PIRS-20 scores. Furthermore, at higher frequencies (gamma, beta and theta bands), EEG power density significantly increased during the Non-Rapid Eye Movement sleep ($p < 0.05$). No statistically significant differences in HRV or actigraphy were detected. Our findings suggest that exposure to a 2.45 GHz radiofrequency device (baby monitor) may impact sleep in some people under real-world conditions however further large-scale real-world investigations with specified dosimetry are required to confirm these findings.

(F, MA) (E) Bobkova NV, Novikov VV, Medvinskaya NI, Aleksandrova IY, Nesterova IV, Fesenko EE. Effect of weak combined static and extremely low-frequency alternating magnetic fields on spatial memory and brain amyloid-β in two animal models of Alzheimer's disease. Electromagn Biol Med. 37(3):127-137, 2018. (AS, CE, BE, CC, MA, ND)

Subchronic effect of a weak combined magnetic field (MF), produced by superimposing a constant component, 42 μT and an alternating MF of 0.08 μT, which was the sum of two frequencies of 4.38 and 4.88 Hz, was studied in olfactory bulbectomized (OBE) and transgenic Tg (APPswe, PSEN1) mice, which were used as animal models of sporadic and heritable Alzheimer's disease (AD) accordingly. Spatial memory was tested in a Morris water maze on the following day after completion of training trials with the hidden platform removed. The amyloid-β (Aβ) level was determined in extracts of the cortex and hippocampus of mice using a specific DOT analysis while the number and dimensions of amyloid plaques were detected after their staining with thioflavin S in transgenic animals. Exposure to the MFs (4 h/day for 10 days) induced the decrease of Aβ level in brain of OBE mice and reduced the number of Aβ plaques in the cortex and hippocampus of Tg animals. However, memory improvement was revealed in Tg mice only, but not in the OBE animals. Here, we suggest that in order to prevent the Aβ accumulation, MFs could be used at early stage of neuronal degeneration in case of AD and other diseases with amyloid protein deposition in other tissues.

(E) Bouisset N, Villard S, Legros A. Vestibular Extremely Low-Frequency Magnetic and Electric Stimulation Effects on Human Subjective Visual Vertical Perception. Bioelectromagnetics 43(6):355-367, 2022. (HU, AE, BE)

Electric fields from both extremely low-frequency magnetic fields (ELF-MF) and alternating current (AC) stimulations impact human neurophysiology. As the retinal photoreceptors, vestibular hair cells are graded potential cells and are sensitive to electric fields. Electrophosphene and magnetophosphene literature suggests different impacts of AC and ELF-MF on the vestibular hair cells. Furthermore, while AC modulates the vestibular system more globally, lateral ELF-MF stimulations could be more utricular specific. Therefore, to further address the impact of ELF-MF-induced electric fields on the human vestibular system and the

potential differences with AC stimulations, we investigated the effects of both stimulation modalities on the perception of verticality using a subjective visual vertical (SVV) paradigm. For similar levels of SVV precision, the ELF-MF condition required more time to adjust SVV, and SVV variability was higher with ELF-MF than with AC vestibular-specific stimulations. Yet, the differences between AC and ELF-MF stimulations were small. Overall, this study highlights small differences between AC and ELF-MF vestibular stimulations, underlines a potential utricular contribution, and has implications for international exposure guidelines and standards.

(F) (E) Brouwer M, Koeman T, van den Brandt PA, Kromhout H, Schouten LJ, Peters S, Huss A, Vermeulen R. Occupational exposures and Parkinson's disease mortality in a prospective Dutch cohort. Occup Environ Med. 72(6):448-455, 2015. (HU, CE, ND)

OBJECTIVES: We investigated the association between six occupational exposures (ie, pesticides, solvents, metals, diesel motor emissions (DME), extremely low frequency magnetic fields (ELF-MF) and electric shocks) and Parkinson's disease (PD) mortality in a large population-based prospective cohort study. METHODS: The Netherlands Cohort Study on diet and cancer enrolled 58 279 men and 62 573 women aged 55-69 years in 1986. Participants were followed up for cause-specific mortality over 17.3 years, until December 2003, resulting in 402 male and 207 female PD deaths. Following a case-cohort design, a subcohort of 5 000 participants was randomly sampled from the complete cohort. Information on occupational history and potential confounders was collected at baseline. Job-exposure matrices were applied to assign occupational exposures. Associations with PD mortality were evaluated using Cox regression. RESULTS: Among men, elevated HRs were observed for exposure to pesticides (eg, ever high exposed, HR 1.27, 95% CI 0.86 to 1.88) and ever high exposed to ELF-MF (HR 1.54, 95% CI 1.00 to 2.36). No association with exposure duration or trend in cumulative exposure was observed for any of the occupational exposures. Results among women were unstable due to small numbers of high-exposed women. CONCLUSIONS: Associations with PD mortality were observed for occupational exposure to pesticides and ELF-MF. However, the weight given to these findings is limited by the absence of a monotonic trend with either duration or cumulative exposure. No associations were found between PD mortality and occupational exposure to solvents, metals, DME or electric shocks.

(F, MA) (E) Bukia N, Butskhrikidze M, Machavariani L, Kekelia G, Svanidze M. POSSIBLE IMPLEMENTATION OF GABAERGIC AND GLUTAMATERGIC SYSTEMS IN REALIZATION OF ANTIEPILEPTIC EFFECTS OF ACOUSTIC RANGE ELECTRO - MAGNETIC FIELDS. Georgian Med News. 280-281:112-116, 2018. (AS, CE, BE, ND, MA)

Seizure is a clinical manifestation of a hyperexcitable neuronal network, in which, the electrical balance underlying the normal neuronal activity is altered pathologically-excitation (Glutamatergic activity) predominates over inhibition (GABAergic activity). Arresting of seizure activity is carried out by restoration of neurotransmitter balance. This process has a direct relation with ion channel permeability in cell and ion transmembrane movement. Low frequency EMS may have a neurostimulating and neuromodulating effect that is based on electromagnetic induction of electric field in the

brain. Under the conditions of certain amplitude, frequency and relaxation time low-frequency electromagnetic field (EMF) induces depolarization of separate neurons, and changes the total cortical excitability in case of repeatedly carried out procedures. It was shown that the exposure of acoustic range EMS in GEPRs treated with GABA-A or GABA-B receptors antagonists decreased behavior seizure activity in response to audiogenic stimuli. Injection of Glutamate receptor agonist on background EMS causes seizure activity, but seizure manifestations have less degree compared to non-stimulated rats. Thus, in response to electromagnetic stimulation, the reduction or complete cramping of seizures can be explained by a change in the activity of the neurotransmitter systems.

(E) Çakıt M O, Koca G, Akbulut A, Erdem O, Çetinkaya S, Umurhan G, Aydınbelge-dizdar N, Esmekaya M, Yumuşak N, Canseven Kurşun AG , Korkmaz M. The effects of extremely low-frequency magnetic field exposure on apoptosis, neurodegeneration and trace element levels in the rat brain. Anatolian Curr Med J / ACMJ / acmj. 5(2): 102-110, 2023. (AS, CE, MC, CC, ND)

Aim: The aim of this study was to investigate the effects of 1mT, 1.5 mT, and 2 mT extremely low-frequency magnetic fields, which were within the limits for public environmental and occupational magnetic field exposure guidelines, on apoptosis, neurodegeneration and trace elements in rat brain cells. Material and Method: A total of 35 adult male Wistar rats were allocated into four main groups: Group 1 (n=8) was healthy controls; Group 2 (n=9) was exposed to 1 mT extremely low-frequency magnetic field; Group 3 (n=9) was exposed to 1.5 mT extremely low-frequency magnetic field and Group 4 (n=9) was exposed to 2 mT extremely low-frequency magnetic field. All the rats in the exposure groups were exposed to 50 Hz extremely low-frequency magnetic field for 4 hours per day, 5 days per week for 30 days in the Helmholtz coils. After the exposure, rats were sacrificed and rat brains were evaluated for histopathological and immunohistochemical changes as well as about the trace element levels in the brain. Results: Different levels of exposure to extremely low-frequency magnetic field doses caused increases in Ca levels and increased apoptosis in the rat brain. As the applied extremely low-frequency magnetic field levels increased, so did the apoptosis and Ca levels in the brain tissues. Conclusion: Extremely low-frequency magnetic field exposure caused neurodegeneration in rat brain tissue, increased apoptosis, and increased Ca concentration. These changes may cause various biological damage, especially cancer in healthy tissues and measures should be taken to minimize extremely low-frequency magnetic field exposure in daily life in terms of protecting public health.

(F) (E) Calabrò E. Competition between hydrogen bonding and protein aggregation in neuronal-like cells under exposure to 50 Hz magnetic field. Int J Radiat Biol. 92:395-402, 2016. (CS, AE, CC)

PURPOSE: To investigate the role of hydrogen bonding and protein unfolding in human SH-SY5Y neuronal-like cells under exposure to a 50 Hz magnetic field (MF) at the intensity of 1 mT. MATERIALS AND METHODS: Neuronal-like cells were placed into an incubator in a 5% CO2/95% air humidified at the temperature of 37.1 °C and exposed

for 4 h to a 50 Hz MF at 1 mT. The exposure system consisted of two Helmholtz coils driven by AC voltage at 50 Hz. Exposed and control samples were studied using Fourier Transform Infrared (FTIR) Spectroscopy. RESULTS: The vibration bands of the methylene group increased significantly after 4 h of exposure. A significant shift to low energies of the Amide I band and an increase in the intensity of the parallel and antiparallel β-sheet structures with respect to the α-helix component were observed after exposure. The Amide II frequency did not change significantly whereas a relative increase of its integrated area with respect to Amide I mode occurred after exposure. CONCLUSIONS: These results can be explained assuming that both the mechanisms of protein aggregation as well as the increase in hydrogen bonding occurred in neuronal-like cells under exposure to a 50 Hz MF.

(F, MA) (E) Calabrò E, Condello S, Magazù S, Ientile, R. Static and 50 Hz electromagnetic fields effects on human neuronal-like cells vibration bands in the mid-infrared region. J Electromagnetic Analysis and Applications 3(2) 69-78, 2011. (CS, AE, CC)

Human neuronal-like cells were exposed to static and 50 Hz electromagnetic fields at the intensities of 2 mT and 1 mT, respectively. The effects of exposure were investigated in the mid-infrared region by means of Fourier self deconvolution spectroscopic analysis. After exposure of 3 hours to static and 50 Hz electromagnetic fields, the vibration bands of CH2 methilene group increased significantly after both exposures, suggesting a relative increase of lipid related to conformational changes in the cell membrane due to electromagnetic fields. In addition, PO2- stretching phosphate bands decreased after both exposures, suggesting that alteration in DNA/RNA can be occurred. In particular, exposure of 3 hours to 50 Hz electromagnetic fields produced significant increases in β-sheet contents in amide I, and around the 1740 cm^{-1} band assigned to non-hydrogen-bonded ester carbonyl stretching mode, that can be related to unfolding processes of proteins structure and cells death. Further exposure up to 18 hours to static magnetic field produced an increase in β-sheet contents as to α-helix components of amide I region, as well.

(F) (E) Calabrò E, Condello S, Currò M, Ferlazzo N, Vecchio M, Caccamo D, Magazù S, Ientile R. 50 Hz Electromagnetic Field Produced Changes in FTIR Spectroscopy Associated with Mitochondrial Transmembrane Potential Reduction in Neuronal-Like SH-SY5Y Cells. Oxid Med Cell Longev. 2013:414393, 2013. (CS, AE, EE)

SH-SY5Y neuroblastoma cells were used as an experimental model to study the effects of 50 Hz electromagnetic field, in the range from 50 μ T to 1.4 mT. Fourier transform infrared spectroscopy analysis evidenced a reduction in intensity of the amide A band and a slight increase of vibration bands at 2921 cm(-1) and 2853 cm(-1) corresponding to methylene groups. A further increase of the magnetic field intensity of exposure up to 0.8 mT and 1.4 mT produced a clear increase in intensity of CH2 vibration bands. Moreover, it has been observed some alterations in the amide I region, such as a shifted peak of the amide I band to a smaller wavenumber, probably due to protein conformational changes. These results suggested that exposure to extremely low electromagnetic fields influenced lipid components of cellular

membrane and the N-H in-plane bending and C-N stretching vibrations of peptide linkages, modifying the secondary structures of α -helix and β -sheet contents and producing unfolding process in cell membrane proteins. The observed changes after exposure to 50 Hz electromagnetic field higher than 0.8 mT were associated with a significant reduction of cell viability and reduced mitochondrial transmembrane potential.

(E) Calderón-Garcidueñas L, Cejudo-Ruiz FR, Stommel EW, González-Maciel A, Reynoso-Robles R, Torres-Jardón R, Tehuacanero-Cuapa S, Rodríguez-Gómez A, Bautista F, Goguitchaichvili A, Pérez-Guille BE, Soriano-Rosales RE, Koseoglu E, Mukherjee PS. Single-domain magnetic particles with motion behavior under electromagnetic AC and DC fields are a fatal cargo in Metropolitan Mexico City pediatric and young adult early Alzheimer, Parkinson, frontotemporal lobar degeneration and amyotrophic lateral sclerosis and in ALS patients. Front Hum Neurosci 18:1411849, 2024. (CE, HU, MC, CC, DE, ND)

Metropolitan Mexico City (MMC) children and young adults exhibit overlapping Alzheimer and Parkinsons' diseases (AD, PD) and TAR DNA-binding protein 43 pathology with magnetic ultrafine particulate matter (UFPM) and industrial nanoparticles (NPs). We studied magnetophoresis, electron microscopy and energy-dispersive X-ray spectrometry in 203 brain samples from 14 children, 27 adults, and 27 ALS cases/controls. Saturation isothermal remanent magnetization (SIRM), capturing magnetically unstable FeNPs ~ 20nm, was higher in caudate, thalamus, hippocampus, putamen, and motor regions with subcortical vs. cortical higher SIRM in MMC ≤ 40y. Motion behavior was associated with magnetic exposures 25-100 mT and children exhibited IRM saturated curves at 50-300 mT associated to change in NPs position and/or orientation *in situ*. Targeted magnetic profiles moving under AC/AD magnetic fields could distinguish ALS vs. controls. Motor neuron magnetic NPs accumulation potentially interferes with action potentials, ion channels, nuclear pores and enhances the membrane insertion process when coated with lipopolysaccharides. TEM and EDX showed 7-20 nm NP Fe, Ti, Co, Ni, V, Hg, W, Al, Zn, Ag, Si, S, Br, Ce, La, and Pr in abnormal neural and vascular organelles. Brain accumulation of magnetic unstable particles start in childhood and cytotoxic, hyperthermia, free radical formation, and NPs motion associated to 30-50 μT (DC magnetic fields) are critical given ubiquitous electric and magnetic fields exposures could induce motion behavior and neural damage. Magnetic UFPM/NPs are a fatal brain cargo in children's brains, and a preventable AD, PD, FTLD, ALS environmental threat. Billions of people are at risk. We are clearly poisoning ourselves.

(F, MA)(NE) Canseven AG, Keskil ZA, Keskil S, Seyhan N. Pentylenetetrazol-induced seizures are not altered by pre- or post-drug exposure to a 50 Hz magnetic field. Radiat Biol. 83(4):231-235, 2007. (AS, AE, BE)

PURPOSE: To investigate whether pre- and post-drug magnetic field (MF) exposure of 50 Hz, 0.2 mT has any significant effect on pentylenetetrazol (PTZ)-induced seizures in mice. MATERIAL AND METHODS: MF was generated by a pair of Helmholtz coils. Seizures were induced by PTZ injection intraperitoneally (i.p.) at a dose of 60 mg/kg. A total of 48 locally bred adult female

mice 25-35 g in weight were used. Latency to seizure, total seizure duration, and mortality were recorded for each mouse. RESULTS: Neither pre- nor post-drug exposure to a 50 Hz, 0.2 mT MF was found to have any effect on PTZ-induced epileptic seizures or mortality rates in mice. CONCLUSION: The present study failed to provide any support for a therapeutic potential of a 50 Hz, 0.2 mT MF for epilepsy.

(F) (E) Capone F, Dileone M, Profice P, Pilato F, Musumeci G, Minicuci G, Ranieri F, Cadossi R, Setti S, Tonali PA, Di Lazzaro V. Does exposure to extremely low frequency magnetic fields produce functional changes in human brain? J Neural Transm. 116(3):257-265, 2009. (HU, FC)

Behavioral and neurophysiological changes have been reported after exposure to extremely low frequency magnetic fields (ELF-MF) both in animals and in humans. The physiological bases of these effects are still poorly understood. In vitro studies analyzed the effect of ELF-MF applied in pulsed mode (PEMFs) on neuronal cultures showing an increase in excitatory neurotransmission. Using transcranial brain stimulation, we studied noninvasively the effect of PEMFs on several measures of cortical excitability in 22 healthy volunteers, in 14 of the subjects we also evaluated the effects of sham field exposure. After 45 min of PEMF exposure, intracortical facilitation produced by paired pulse brain stimulation was significantly enhanced with an increase of about 20%, while other parameters of cortical excitability remained unchanged. Sham field exposure produced no effects. The increase in paired-pulse facilitation, a physiological parameter related to cortical glutamatergic activity, suggests that PEMFs exposure may produce an enhancement in cortical excitatory neurotransmission. This study suggests that PEMFs may produce functional changes in human brain.

(F) (E) Carrasco-López C, Soto-León V, Céspedes V, Profice P, Strange BA, Foffani G, Oliviero A. Static Magnetic Field Stimulation over Parietal Cortex Enhances Somatosensory Detection in Humans. J Neurosci. 37(14):3840-3847, 2017. (HU, AE, EE, BE)

The role of neuronal oscillations in human somatosensory perception is currently unclear. To address this, here we use noninvasive brain stimulation to artificially modulate cortical network dynamics in the context of neurophysiological and behavioral recordings. We demonstrate that transcranial static magnetic field stimulation (tSMS) over the somatosensory parietal cortex increases oscillatory power specifically in the alpha range, without significantly affecting bottom-up thalamocortical inputs indexed by the early cortical component of somatosensory evoked potentials. Critically, we next show that parietal tSMS enhances the detection of near-threshold somatosensory stimuli. Interestingly, this behavioral improvement reflects a decrease of habituation to somatosensation. Our data therefore provide causal evidence that somatosensory perception depends on parietal alpha activity.SIGNIFICANCE STATEMENT Artificially increasing alpha power by placing a powerful magnetic field over the somatosensory cortex overcomes the natural decline in detection probability of a repeated near-threshold sensory stimulus.

(E) Carrillo-Márquez JR, Carrillo-Márquez MF, Ceniceros-Obregón A, Gómez-Apo E, Escobar-España A, Rodríguez-Serrano LM, Carrillo-Ruiz JD. Electromagnetic field stimulation for long-term mobility assessment after sciatic nerve injury. Neurol Res. DOI: 10.1080/01616412.2025.2504715. (AS, CE, FC. MA)

Introduction: Gauss (G) or miliTesla (mT) units measure electromagnetic field (EMF) stimulation. Tarlov Scale (TS) assesses motor impairment, Finger Abduction Scale (FAS) measures finger separation. The objective is to evaluate mobility using EMF in a Sciatic Nerve Injury (SNI) model. **Materials & methods:** SNI caused paresis in the right hind limb to observe motor changes in male Sprague-Dawley rats (372-529 g) ($N = 30$). Three groups of ($n = 10$) rats were created. Control Group (CG) was just injured. The experimental groups were EMF-treated two hours a day for four weeks (2/24, 5/7, 4/4), applying Gauss intensities: Low-Intensity (LIMF) 60-100 (6-10 mT) & High-Intensity (HIMF) 140-200 (14-20 mT). The mobility was measured each week with TS & FAS. Sciatic nerve & skeletal muscle histological slides were made with traditional staining technique to evaluate cellular inflammation. We used two-tailed repeated ANOVA measures & Bonferroni *post hoc* tests, with a significance $p < 0.05$ ($\alpha = 0.05$) and $\beta = 80\%$. **Results:** EMFs effectively treat SNI in rats, improving the mobility of the right hind limb in experimental groups. In the last week, TS scores were CG 3.5 (±1.35) $p = 0.006$, LIMF 4 (±0) $p = 0.0001$ & HIMF 4.3 (±0.82) $p = 0.02$. FAS scores were CG 0.2 (±0.42) $p = 0.000001$, LIMF 1.5 (±0.70) $p = 0.05$ & HIMF 1.8 (±0.42) $p = 0.1$. In histological findings, CG had inflammation in nerve & muscle, LIMF & HIMF diminished cellular activity.
Discussion: TS & FAS helped to improve mobility in experimental groups using EMFs after SNI. The nerve repairing mechanism should be studied in future models.

(E) Carrubba S, Frilot C 2nd, Chesson AL Jr, Marino AA. Mobile-phone pulse triggers evoked potentials. Neurosci Lett. 469(1):164-168, 2010. (HU, EE)

If mobile-phone electromagnetic fields (EMFs) are hazardous, as suggested in the literature, processes or mechanisms must exist that allow the body to detect the fields. We hypothesized that the low-frequency pulses produced by mobile phones (217 Hz) were detected by sensory transduction, as evidenced by the ability of the pulses to trigger evoked potentials (EPs). Electroencephalograms (EEGs) were recorded from six standard locations in 20 volunteers and analyzed to detect brain potentials triggered by a pulse of the type produced by mobile phones. Evoked potentials having the expected latency were found in 90% of the volunteers, as assessed using a nonlinear method of EEG analysis. Evoked potentials were not detected when the EEG was analyzed using time averaging. The possibility of systematic error was excluded by sham-exposure analyses. <u>The results implied that mobile-phones trigger EP at the rate of 217 Hz during ordinary phone use. Chronic production of the changes in brain activity might be pertinent to the reports of health hazards among mobile-phone users.</u>

(E) Carrubba S, Frilot C, Chesson AL, Marino AA. Nonlinear EEG activation evoked by low-strength low-frequency magnetic fields. Neurosci Lett. 417(2):212-216, 2007. (HU, AE, EE)

Recent electrophysiological evidence suggested the existence of a human magnetic sense, but the kind of dynamical law that governed the stimulus-response relationship was not

established. We tested the hypothesis that brain potentials evoked by the onset of a weak, low-frequency magnetic field were nonlinearly related to the stimulus. A field of 1G, 60 Hz was applied for 2s, with a 5s inter-stimulus period, and brain potentials were recorded from occipital electrodes in eight subjects, each of whom were measured twice, with at least 1 week between measurements. The recorded signals were subjected to nonlinear (recurrence analysis) and linear (time averaging) analyses. Using recurrence analysis, magnetosensory evoked potentials (MEPs) were detected in each subject in both the initial and replicate studies, with one exception. All MEPs exhibited the expected latency but differed in dynamical characteristics, indicating that they were nonlinearly related to the stimulus. MEPs were not detected using time averaging, thereby further confirming their nonlinearity. Evolutionarily conditioned structures that help mediate linear field-transduction in lower life forms may be expressed and functionally utilized in humans, but in a role where they facilitate vulnerability to man-made environmental fields.

(E) Cason AM, Denbleyker M, Ferrence K, Smith JC, Houpt TA. Sex and estrous cycle differences in the behavioral effects of high-strength static magnetic fields: role of ovarian steroids. Am J Physiol Regul Integr Comp Physiol 290(3):R659-67, 2006. (AS, AE, BE)

Advances in magnetic resonance imaging are driving the development of higher-resolution machines equipped with high-strength static magnetic fields (MFs). The behavioral effects of high-strength MFs are largely uncharacterized, although in male rats, exposure to 7 T or above induces locomotor circling and leads to a conditioned taste avoidance (CTA) if paired with a novel taste. Here, the effects of MFs on male and female rats were compared to determine whether there are sex differences in behavioral responses and whether these can be explained by ovarian steroid status. Rats were given 10-min access to a novel saccharin solution and then restrained within a 14-T magnet for 30 min. Locomotor activity after exposure was scored for circling and rearing. CTA extinction was measured with two-bottle preference tests. In experiment 1, males were compared with females across the estrous cycle after a single MF exposure. Females circled more and acquired a more persistent CTA than males; circling was highest on the day of estrus. In experiment 2, the effects of three MF exposures were compared among intact rats, ovariectomized females, and ovariectomized females with steroid replacement. Compared with intact rats, ovariectomy increased circling; estrogen replacement blocked the increase. Males acquired a stronger initial CTA but extinguished faster than intact or ovariectomized females. Thus the locomotor circling induced by MF exposure was increased in females and modulated by ovarian steroids across the estrous cycle and by hormone replacement. Furthermore, female rats acquired a more persistent CTA than male rats, which was not dependent on estrous phase or endogenous ovarian steroids.

(E) Cason AM, Kwon B, Smith JC, Houpt TA. Labyrinthectomy abolishes the behavioral and neural response of rats to a high-strength static magnetic field. Physiol Behav 97(1):36-43, 2009. (AS, AE, BE)

Vertigo is a commonly-reported side effect of exposure to the high magnetic fields found in magnetic resonance imaging machines. Although it has been hypothesized that high magnetic fields interact with the vestibular apparatus of the inner ear, there has been no direct evidence establishing its role in magnet-induced vertigo. Our laboratory has shown that following

exposure to high magnetic fields, rats walk in circles, acquire a conditioned taste aversion (CTA), and express c-Fos in vestibular and visceral relays of the brainstem, consistent with vestibular stimulation and vertigo or motion sickness. To determine if the inner ear is required for these effects, rats were chemically labyrinthectomized with sodium arsanilate and tested for locomotor circling, CTA acquisition, and c-Fos induction after exposure within a 14.1 T magnet. Intact rats circled counterclockwise after 30-min exposure to 14.1 T, but labyrinthectomized rats showed no increase in circling after magnetic field exposure. After 3 pairings of 0.125% saccharin with 30-min exposure at 14.1 T, intact rats acquired a profound CTA that persisted for 14 days of extinction testing; labyrinthectomized rats, however, did not acquire a CTA and showed a high preference for saccharin similar to sham-exposed rats. Finally, significant c-Fos was induced in the brainstem of intact rats by 30-min exposure to 14.1 T, but magnetic field exposure did not elevate c-Fos in labyrinthectomized rats above sham-exposed levels. These results demonstrate that an intact inner ear is necessary for all the observed effects of exposure to high magnetic fields in rats.

(E) Celik MS, Guven K, Akpolat V, Akdag MZ, Naziroglu M, Gul-Guven R, Celik MY, Erdogan S. Extremely low-frequency magnetic field induces manganese accumulation in brain, kidney and liver of rats. Toxicol Ind Health. 31(6):576-580, 2015. (AS, CE, CC)

The aim of the present study was to determine the effects of extremely low-frequency magnetic field (ELF-MF) on accumulation of manganese (Mn) in the kidney, liver and brain of rats. A total of 40 rats were randomly divided into eight groups. Four control groups received 0, 3.75, 15 and 60 mg Mn per kg body weight orally every 2 days for 45 days, respectively. The remaining four groups received same concentrations of Mn and were also exposed to ELF-MF (1.5 mT; 50 Hz) for 4 h for 5 days a week during 45 days. Following the last exposure, kidney, liver and brain were taken from all rats and they were analyzed for Mn accumulation levels using an inductively coupled plasma-optical emission spectrometer. In result of the current study, we observed that Mn levels in brain, kidney and liver were higher in Mn groups than in control groups. Mn levels in brain, kidney and liver were also higher in Mn plus ELF-MF groups than in Mn groups. In conclusion, result of the current study showed that the ELF-MF induced manganese accumulation in kidney, liver and brain of rats.

(E) Che Y, Sun H, Cui Y, Zhou D, Ma Y. Effects of exposure to 50 Hz magnetic field of 1 mT on the performance of detour learning task by chicks. Brain Res Bull. 74(1-3):178-182, 2007. (AS, CE, BE)

In the present study, we examined the effects of exposure to an extremely low-frequency magnetic field of 1 mT intensity on learning and memory in Lohmann brown domestic chicks using detour learning task. These results show that 20 h/day exposure to a low-frequency magnetic field induces a significant impairment in detour learning but 50 min/day exposure has no effect.

(E) Cheng L, Yang B, Du H, Zhou T, Li Y, Wu J, Cao Z, Xu A. Moderate intensity of static magnetic fields can alter the avoidance behavior and fat storage of Caenorhabditis

elegans via serotonin. Environ Sci Pollut Res Int 29(28):43102-43113, 2022. (AS, AE, BE, CC)

Man-made static magnetic fields (SMFs) widely exist in human life as a physical environmental factor. However, the biological responses to moderate SMFs exposure and their underlying mechanisms are largely unknown. The present study was focused on exploring the nervous responses to moderate-intensity SMFs at 0.5 T and 1 T in Caenorhabditis elegans (C. elegans). We found that SMFs at either 0.5 T or 1 T had no statistically significant effects on the locomotor behaviors, while the 1 T magnetic field increased pharyngeal pumping. The avoidance behavior of the pathogenic Pseudomonas aeruginosa was greatly decreased in either 0.5 T or 1 T SMFs exposed nematodes, and the learning index was reducede from 0.52 ± 0.11 to 0.23 ± 0.17 and 0.16 ± 0.11, respectively. The total serotonin level was increased by 17.08% and 16.45% with the treatment of 0.5 T and 1 T SMF, compared to the control group; however, there were minimal effects of SMFs on other three neurotransmitters including choline, γ-aminobutyric acid (GABA), dopamine. RT-qPCR was used to further investigate the expression of serotonin-related genes, including rate-limiting enzymes, transcription factors and transport receptors. The expression levels of tph-1 and unc-86 genes were increased by SMF exposure, while those of ocr-2, osm-9, ser-1 and mod-1 genes were decreased. With the staining of lipid in either wild-type N2 or tph-1 mutants, we found that 0.5 T and 1 T SMFs decreased fat storage in C. elegans via serotonin pathway. Our study demonstrated that moderate-intensity SMFs induced neurobehavioral disorder and the reduction of fat storage by disturbing the secretion of serotonin in C. elegans, which provided new insights into elucidating nervous responses of C. elegans to moderate-intensity SMFs.

(E) Cheng Y, Dai Y, Zhu X, Xu H, Cai P, Xia R, Mao L, Zhao BQ, Fan W. Extremely low-frequency electromagnetic fields enhance the proliferation and differentiation of neural progenitor cells cultured from ischemic brains. Neuroreport. 26(15):896-902, 2015. (CS, CE, FC, MA)

In the mammalian brain, neurogenesis persists throughout the embryonic period and adulthood in the subventricular zone of the lateral ventricle and the granular zone (dentate gyrus) of the hippocampus. Newborn neural progenitor cells (NPCs) in the two regions play a critical role in structural and functional plasticity and neural regeneration after brain injury. Previous studies have reported that extremely low-frequency electromagnetic fields (ELF-EMF) could promote osteogenesis, angiogenesis, and cardiac stem cells' differentiation, which indicates that ELF-EMF might be an effective tool for regenerative therapy. The present studies were carried out to examine the effects of ELF-EMF on hippocampal NPCs cultured from embryonic and adult ischemic brains. We found that exposure to ELF-EMF (50 Hz, 0.4 mT) significantly enhanced the proliferation capability both in embryonic NPCs and in ischemic NPCs. Neuronal differentiation was also enhanced after 7 days of cumulative ELF-EMF exposure, whereas glial differentiation was not influenced markedly. The expression of phosphorylated Akt increased during the proliferation process when ischemic NPCs were exposed to ELF-EMF. However, blockage of the Akt pathway abolished the ELF-EMF-induced proliferation of ischemic NPCs. These data show that ELF-EMF promotes

neurogenesis of ischemic NPCs and suggest that this effect may occur through the Akt pathway.

(E) Chicas-Mosier AM, Radi M, Lafferrandre J, O'Hara JF, Vora HD, Abramson CI. Low Strength Magnetic Fields Serve as a Cue for Foraging Honey Bees but Prior Experience is More Indicative of Choice. Bioelectromagnetics 41(6):458-470, 2020. (AS, AE, BE)

Species of migrating insects use magnetic fields as a navigational tool that is independent of current weather conditions and non-migrating species have been shown to discriminate anomalies in magnetic field from the earth's baseline. Honey bee discrimination of magnetic field has been studied in the context of associative learning, physiology, and whole hive responses. This article uses a combination of free-flight and laboratory studies to determine how small fluctuations from Earth's magnetic field affect honey bee (Apis mellifera L.) decision-making. Honey bees were tested in three experiments: (i) recruitment to an aqueous sucrose feeder, (ii) an artificial free-flight flower patch with floral color-dependent magnetic field strength, and (iii) a Y-maze with alternating colors on a stronger magnetic field. In free-flying feeder experiments, magnetic field served as a temporary cue, but when offered an equal caloric alternative with lesser magnetic field, the latter was preferred. Flower patch experiments showed initial color biases that were abandoned as a response to magnetic field induction. In laboratory experiments, bees showed a color-dependent behavioral response to the magnetic field. The results of this study indicate that bees may use small fluctuations in magnetic fields as a cue but that it is likely low-value as compared with other stimuli.

(E) Cho H, Seo YK, Yoon HH, Kim SC, Kim SM, Song KY, Park JK. Neural stimulation on human bone marrow-derived mesenchymal stem cells by extremely low frequency electromagnetic fields (ELF-EMFs). Biotechnol Prog. 28:1329-1335, 2012. (CS, CE, MC, DE, MA)

Adult stem cells are considered to be multipotent.Especially,human bone marrow-derived mesenchymal stem cells (hBM-MSCs) have the potential to differentiate into nerve type cells. Electromagnetic fields (EMFs) are widely distributed in the environment, and recently there have been many reports on the biological effects of EMFs. hBM-MSCs are weak and sensitive pluripotent stem cells, therefore extremely low frequency- electromagnetic fields (ELF-EMFs) could be affect the changes of biological functions within the cells. In our experiments, ELF-EMFs inhibited the growth of hBM-MSCs in 12 days exposure. Their gene level was changed and expression of the neural stem cell marker like nestin was decreased but the neural cell markers like MAP2, NEUROD1, NF-L and Tau were induced. In immunofluorescence study, we confirmed the expression of each protein of neural cells. And also both oligodendrocyte and astrocyte related proteinslike O4 and GFAP were expressed by ELF-EMFs. **We suggest that EMFs can induce neural differentiation in BM-MSCs without any chemicals or differentiation factors.**

(E) Cho SI, Nam YS, Chu LY, Lee JH, Bang JS, Kim HR, Kim HC, Lee YJ, Kim HD, Sul JD, Kim D, Chung YH, Jeong JH. Extremely low-frequency magnetic fields modulate nitric oxide signaling in rat brain. Bioelectromagnetics. 33(7):568-574, 2012. (AS, CE, CC, OX)

Our previous study has shown that an extremely low-frequency magnetic field (ELF-MF) induces nitric oxide (NO) synthesis by Ca(2+) -dependent NO synthase (NOS) in rat brain. The present study was designed to confirm that ELF-MF affects neuronal NOS (nNOS) in several brain regions and to investigate the correlation between NO and nNOS activation. The exposure of rats to a 2 mT, 60 Hz ELF-MF for 5 days resulted in increases of NO levels in parallel with cGMP elevations in the cerebral cortex, striatum, and hippocampus. Cresyl violet staining and electron microscopic evaluation revealed that there were no significant differences in the morphology and number of neurons in the cerebral cortex, striatum, and hippocampus. Differently, the numbers of nNOS-immunoreactive (IR) neurons were significantly increased in those cerebral areas in ELF-MF-exposed rats. These data suggest that the increase in NO could be due to the increased expression and activation of nNOS in cells. Based on NO signaling in physiological and pathological states, ELF-MF created by electric power systems may induce various physiological changes in modern life.

Choi EH, Nwakalor C, Brown NJ, Lee J, Oh MY, Yang IH. Therapeutic potential of neuromodulation for demyelinating diseases. Neural Regen Res 16(2):214-217, 2021. (Review)

Neuromodulation represents a cutting edge class of both invasive and non-invasive therapeutic methods which alter the activity of neurons. Currently, several different techniques have been developed - or are currently being investigated - to treat a wide variety of neurological and neuropsychiatric disorders. Recently, in vivo and in vitro studies have revealed that neuromodulation can also induce myelination, meaning that it could hold potential as a therapy for various demyelinating diseases including multiple sclerosis and progressive multifocal leukencepalopathy. These findings come on the heels of a paradigm shift in the view of myelin's role within the nervous system from a static structure to an active co-regulator of central nervous system plasticity and participant in neuron-mediated modulation. In the present review, we highlight several of the recent findings regarding the role of neural activity in altering myelination including several soluble and contact-dependent factors that seem to mediate neural activity-dependent myelination. We also highlight several considerations for neuromodulatory techniques, including the need for further research into spatiotemporal precision, dosage, and the safety and efficacy of transcranial focused ultrasound stimulation, an emerging neuromodulation technology. As the field of neuromodulation continues to evolve, it could potentially bring forth methods for the treatment of demyelinating diseases, and as such, further investigation into the mechanisms of neuron-dependent myelination as well as neuro-imaging modalities that can monitor myelination activity is warranted.

(E) Choi YK, Lee DH, Seo YK, Jung H, Park JK, Cho H. Stimulation of neural differentiation in human bone marrow mesenchymal stem cells by extremely low-frequency electromagnetic fields incorporated with MNPs. Appl Biochem Biotechnol. 174:1q33-1245, 2014. (CS, AE, MC, MA)

Human bone marrow-derived mesenchymal stem cells (hBM-MSCs) have been investigated as a new cell-therapeutic solution due to their capacity that could differentiate into neural-like cells. Extremely low-frequency electromagnetic fields (ELF-EMFs) therapy has emerged as a novel technique, using mechanical stimulus to differentiate hBM-MSCs and significantly enhance neuronal differentiation to affect cellular and molecular reactions. Magnetic iron oxide (Fe_3O_4) nanoparticles (MNPs) have recently achieved widespread use for biomedical applications and polyethylene glycol (PEG)-labeled nanoparticles are used to increase their circulation time, aqueous solubility, biocompatibility, and nonspecific cellular uptake as well as to decrease immunogenicity. Many studies have used MNP-labeled cells for differentiation, but there have been no reports of MNP-labeled neural differentiation combined with EMFs. In this study, synthesized PEG-phospholipid encapsulated magnetite (Fe_3O_4) nanoparticles are used on hBM-MSCs to improve their intracellular uptake. The PEGylated nanoparticles were exposed to the cells under 50 Hz of EMFs to improve neural differentiation. First, we measured cell viability and intracellular iron content in hBM-MSCs after treatment with MNPs. Analysis was conducted by RT-PCR, and immunohistological analysis using neural cell type-specific genes and antibodies after exposure to 50 Hz electromagnetic fields. These results suggest that electromagnetic fields enhance neural differentiation in hBM-MSCs incorporated with MNPs and would be an effective method for differentiating neural cells.

(E) Choi Y-K, Urnukhsaikhan E, Yoon H-H, Seo Y-K, Park J-K. Effect of human mesenchymal stem cell transplantation on cerebral ischemic volume-controlled photothrombotic mouse model. Biotechnol J 11(11):1397-1404, 2016. (AS, CE, MC FC, MA)

Various animal models of stroke have been developed to simulate the human stroke with the development of the ischemic method facilitates preclinical stroke research. The photothrombotic ischemia model, based on the intravascular photochemical reaction, is widely used for in vivo studies. However, this study has limitations, which generated a relatively small-sized infarction model on superficial cortex compared to that of the MCAO stroke model. In this study, the photothorombosis mouse model is adapted and the optimum conditions for generation of cell death and deficits with high reproducibility is determined. The extent of damage within the cortex was assessed by infarct volume and cellular/behavioral analyses. In this model, the neural cell death and inflammatory responses is detected; moreover, the degree of behavioral impairment is correlated with the brain infarct volume. Further, to enhance the understanding of neural repair, the effect of neural differentiation by transplantation of human bone marrow-derived mesenchymal stem cells (BM-MSCs) is analyzed. The authors demonstrated that transplantation of BM-MSCs promoted the neural differentiation and behavioral performance in their photothrombosis model. Therefore, this research was meaningful to provide a stable animal model of stroke with low variability. Moreover, this model will facilitate development of novel MSC-based therapeutics for stroke.

(E) Choi Y-K, Urnukhsaikhan E, Yoon H-H, Seo Y-K, Cho H, Jeong J-S, Kim S-C, Jung-Keug Park J-K. Combined effect of pulsed electromagnetic field and sound wave on In vitro and In vivo neural differentiation of human mesenchymal stem cells. Biotechnol Prog 33(1):201-211, 2017. (AS, CS, CE, AE, MC, MA)

Biophysical wave stimulus has been used as an effective tool to promote cellular maturation and differentiation in the construction of engineered tissue. Pulsed electromagnetic fields (PEMFs) and sound waves have been selected as effective stimuli that can promote neural differentiation. The aim of this study was to investigate the synergistic effect of PEMFs and sound waves on the neural differentiation potential in vitro and in vivo using human bone marrow mesenchymal stem cells (hBM-MSCs). In vitro, neural-related genes in hBM-MSCs were accelerated by the combined exposure to both waves more than by individual exposure to PEMFs or sound waves. The combined wave also up-regulated the expression of neural and synaptic-related proteins in a three-dimensional (3-D) culture system through the phosphorylation of extracellular signal-related kinase. In a mouse model of photochemically induced ischemia, exposure to the combined wave reduced the infarction volume and improved post-injury behavioral activity. These results indicate that a combined stimulus of biophysical waves, PEMFs and sound can enhance and possibly affect the differentiation of MSCs into neural cells. Our study is meaningful for highlighting the potential of combined wave for neurogenic effects and providing new therapeutic approaches for neural cell therapy.

(E) Chu LY, Lee JH, Nam YS, Lee YJ, Park WH, Lee BC, Kim D, Chung YH, Jeong JH. Extremely low frequency magnetic field induces oxidative stress in mouse cerebellum. Gen Physiol Biophys. 30(4):415-421, 2011. (AS, CE, OX)

We have investigated whether extremely low frequency magnetic field (ELF-MF) induces lipid peroxidation and reactive oxygen species in mouse cerebellum. After exposure to 60 Hz ELF-MF at 2.3 mT intensity for 3 hours, there was a significant increase in malondialdehyde level and hydroxyl radical. ELF-MF significantly induced concomitant increase in superoxide dismutase without alteration in glutathione peroxidase activity. While glutathione contents were not altered, ascorbic acid levels were significantly decreased by ELF-MF exposure. These results indicate that ELF-MF may induce oxidative stress in mouse cerebellum. However, the mechanism remains further to be characterized.

(E) Chung YH, Lee YJ, Lee HS, Chung SJ, Lim CH, Oh KW, Sohn UD, Park ES, Jeong JH. Extremely low frequency magnetic field modulates the level of neurotransmitters. Korean J Physiol Pharmacol. 19(1):15-20, 2015. (AS, CE, CC, OX)

This study was aimed to observe that extremely low frequency magnetic field (ELF-MF) may be relevant to changes of major neurotransmitters in rat brain. After the exposure to ELF-MF (60 Hz, 2.0 mT) for 2 or 5 days, we measured the levels of biogenic amines and their metabolites, amino acid neurotransmitters and nitric oxide (NO) in the cortex, striatum, thalamus, cerebellum and hippocampus. The exposure of ELF-MF for 2 or 5 days produced significant differences in norepinephrine and vanillyl mandelic acid in the striatum, thalamus, cerebellum and hippocampus. Significant increases in the levels of serotonin and 5-hydroxyindoleacetic acid were also observed in the striatum, thalamus or hippocampus. ELF-MF significantly increased the concentration of dopamine in the thalamus. ELF-MF tended to increase the levels of amino acid neurotransmitters such as glutamine, glycine and γ -aminobutyric acid in the striatum and thalamus, whereas it decreased the levels in the cortex, cerebellum and hippocampus. ELF-MF significantly increased NO concentration in the striatum, thalamus and hippocampus. The present study has demonstrated that exposure to ELF-MFs may evoke the changes in the levels

of biogenic amines, amino acid and NO in the brain although the extent and property vary with the brain areas. However, the mechanisms remain further to be characterized.

(E) Cichoń N, Bijak M, Miller E, Saluk J. Extremely low frequency electromagnetic field (ELF-EMF) reduces oxidative stress and improves functional and psychological status in ischemic stroke patients. Bioelectromagnetics. 38(5):386-396, 2017. (HU, CE, OX, BE, MA)

As a result of ischaemia/reperfusion, massive generation of reactive oxygen species occurs, followed by decreased activity of antioxidant enzymes. Extremely low frequency electromagnetic fields (ELF-EMF) can modulate oxidative stress, but there are no clinical antioxidant studies in brain stroke patients. The aim of our study was to investigate the effect of ELF-EMF on clinical and antioxidant status in post-stroke patients. Fifty-seven patients were divided into two groups: ELF-EMF and non-ELF-EMF. Both groups underwent the same 4-week rehabilitation program. Additionally, the ELF-EMF group was exposed to an ELF-EMF field of 40 Hz, 7 mT for 15 min/day for 4 weeks (5 days a week). The activity of catalase and superoxide dismutase was measured in hemolysates, and total antioxidant status (TAS) determined in plasma. Functional status was assessed before and after the series of treatments using Activities of Daily Living (ADL), Mini-Mental State Examination (MMSE), and Geriatric Depression Scale (GDS). Applied ELF-EMF significantly increased enzymatic antioxidant activity; however, TAS levels did not change in either group. Results show that ELF-EMF induced a significant improvement in functional (ADL) and mental (MMSE, GDS) status. Clinical parameters had positive correlation with the level of enzymatic antioxidant protection.

(E) Cichoń N, Czarny P, Bijak M, Miller E, Śliwiński T, Szemraj J, Saluk-Bijak J. Benign Effect of Extremely Low-Frequency Electromagnetic Field on Brain Plasticity Assessed by Nitric Oxide Metabolism during Poststroke Rehabilitation. Oxid Med Cell Longev. 2017:2181942, 2017b. (HU, CE, OX, FC, MA)

Nitric oxide (NO) is one of the most important signal molecules, involved in both physiological and pathological processes. As a neurotransmitter in the central nervous system, NO regulates cerebral blood flow, neurogenesis, and synaptic plasticity. The aim of our study was to investigate the effect of the extremely low-frequency electromagnetic field (ELF-EMF) on generation and metabolism of NO, as a neurotransmitter, in the rehabilitation of poststroke patients. Forty-eight patients were divided into two groups: ELF-EMF and non-ELF-EMF. Both groups underwent the same 4-week rehabilitation program. Additionally, the ELF-EMF group was exposed to an extremely low-frequency electromagnetic field of 40 Hz, 7 mT, for 15 min/day. Levels of 3-nitrotyrosine, nitrate/nitrite, and TNFα in plasma samples were measured, and NOS2 expression was determined in whole blood samples. Functional status was evaluated before and after a series of treatments, using the Activity Daily Living, Geriatric Depression Scale, and Mini-Mental State Examination. We observed that application of ELF-EMF significantly increased 3-nitrotyrosine and nitrate/nitrite levels, while expression of NOS2 was insignificantly decreased in both groups. The results also show that ELF-EMF treatments improved functional and mental status. We conclude that ELF-EMF therapy is capable of promoting recovery in poststroke patients.

(E) Cichoń N, Bijak M, Czarny P, Miller E, Synowiec E, Sliwinski T, Saluk-Bijak J. Increase in Blood Levels of Growth Factors Involved in the Neuroplasticity Process by Using an Extremely Low Frequency Electromagnetic Field in Post-stroke Patients. Front Aging Neurosci. 10:294, 2018. (HU, CE, BE, CC, MA)

Background: Neuroplasticity ensures the improvement of functional status in patients after stroke. The aim of this study was to evaluate the effect of extremely low-frequency electromagnetic field therapy (ELF-EMF) on brain plasticity in the rehabilitation of patients after stroke. Methods: Forty-eight patients were divided into two groups underwent the same rehabilitation program, but in the study group, the patients additionally were exposed to a standard series of 10 ELF-EMF treatments. To determine the level of neuroplasticity, we measured the plasma level of the brain-derived neurotrophic factor (BDNF), the vascular-endothelial growth factor, as well as BDNF mRNA expression. Additionally, we determined the molecule levels for hepatocyte growth factor, stem cell factor, stromal cell-derived factor 1α, nerve growth factor β, and leukemia inhibitory factor, using 5plex cytokine panel in plasma. After 4 weeks, during which patients had undergone neurorehabilitation and neurological examinations, we assessed functional recovery using the Barthel Index, Mini-Mental State Examination (MMSE), Geriatric Depression Scale, National Institutes of Health Stroke Scale (NIHSS), and the modified Rankin Scale (mRS). Results: We observed that ELF-EMF significantly increased growth factors and cytokine levels involved in neuroplasticity, as well as promoted an enhancement of functional recovery in post-stroke patients. Additionally, we presented evidence that these effects could be related to the increase of gene expression on the mRNA level. Moreover, a change of BDNF plasma level was positively correlated with the Barthel Index, MMSE, and negatively correlated with GDS. Conclusion: Extremely low-frequency electromagnetic field therapy improves the effectiveness of rehabilitation of post-stroke patients by improving neuroplasticity processes.

(E) Cichon N, Bijak M, Synowiec E, Miller E, Sliwinski T, Saluk-Bijak J. Modulation of antioxidant enzyme gene expression by extremely low frequency electromagnetic field in post-stroke patients. Scand J Clin Lab Invest. 78(7-8):626-631, 2018. (HU, CE, OX, MA)

Oxidative stress plays the most important role in the pathogenesis of stroke. Extremely low frequency electromagnetic field (ELF-EMF) therapy may be complementary in post-stroke therapy, as it modulates oxidative stress. The aim of this study was to evaluate the messenger ribonucleic acid (mRNA) levels of certain antioxidant genes in post-stroke patients given ELF-EMF therapy. Forty-eight post-stroke patients were divided into two groups: an ELF-EMF group and a non-ELF-EMF group. All patients underwent the same program of physical therapy, but the ELF-EMF group was additionally given ELF-EMF treatment. In order to determine the level of gene expression, we evaluated the level of mRNA expression of catalase, superoxide dismutase, and glutathione peroxidase. We observed that after ELF-EMF therapy, the mRNA expression of the studied genes (CAT, SOD1, SOD2, GPx1, and GPx4) significantly increased, which enhanced the antioxidant defence of the body. ELF-EMF therapy intensifies the endogenous antioxidant system by increasing the mRNA expression of genes encoding antioxidant enzymes and enhances the effectiveness of post-stroke patient therapy.

(E) Cichoń N, Rzeźnicka P, Bijak M, Miller E, Miller S, Saluk J. Extremely low frequency electromagnetic field reduces oxidative stress during the rehabilitation of post-acute stroke patients. Adv Clin Exp Med. 27(9):1285-1293, 2018. (HU, CE, BE, OX, MA)

BACKGROUND: One of the therapeutic methods used in stroke rehabilitation is magnetotherapy using extremely low frequency and variable pulse shape electromagnetic field (ELF-EMF). OBJECTIVES: The aim of our study was to investigate the effect of magnetotherapy on the condition of postacute stroke patients, as measured by plasma oxidative stress markers and clinical parameters which show the progress of rehabilitation. MATERIAL AND METHODS: The selected 57 post-stroke patients were divided into 2 groups, those with ELFEMF therapy and those without. The level of oxidative stress in the plasma was estimated by typical markers: thiobarbituric acid reactive substances (TBARS), thiol groups, and carbonyl groups. The effect of ELF-EMF on the course of the patients' rehabilitation following ischemic stroke was evaluated with the use of scales of physical activity and mental state: Activities of Daily Living (ADL), Mini-Mental State Examination (MMSE) and Geriatric Depression Scale (GDS). RESULTS: Our comparative analysis showed that all parameters of oxidative stress are significantly reduced during rehabilitation using ELF-EMF, compared to the control group rehabilitated only by kinesiotherapy. We also recorded much higher therapeutic benefits using magnetotherapy, which revealed a significant improvement of clinimetric parameters. CONCLUSIONS: The ELF-EMF therapy meaningfully improves the overall condition of patients through a decrease of oxidative stress markers and it significantly affects the psychophysical abilities of patients after stroke. The change in carbonyl group level correlates with the change in the degree of physical and mental disability; therefore, it could be a marker for the effectiveness of rehabilitation.

(E) Cichon N, Synowiec E, Miller E, Sliwinski T, Ceremuga M, Saluk-Bijak J, Bijak M Effect of Rehabilitation with Extremely Low Frequency Electromagnetic Field on Molecular Mechanism of Apoptosis in Post-Stroke Patients. Brain Sci 10(5):266 2020. (HU, CE, CC, ND)

Apoptosis in acute stroke is associated with a negative prognosis and is correlated with the severity of the neurological deficit. However, there is no evidence that indicates that, in the subacute phase of the stroke, the apoptosis process might activate neuroplasticity. Therefore, in this study, we investigated the effect of an extremely low frequency electromagnetic field (ELF-EMF) on the molecular mechanism of apoptosis, as used in the rehabilitation of post-stroke patients. Patients with moderate stroke severity (n = 48), 3-4 weeks after incident, were enrolled in the analysis and divided into ELF-EMF and non-ELF-EMF group. The rehabilitation program in both groups involves the following: kinesiotherapy-30 min; psychological therapy-15 min; and neurophysiological routines-60 min. Additionally, the ELF-EMF group was exposed to an ELF-EMF (40 Hz, 5 mT). In order to assess the apoptosis gene expression level, we measured the mRNA expression of *BAX*, *BCL-2*, *CASP8*, *TNFα*, and *TP53*. We found that ELF-EMF significantly increased the expression of *BAX*, *CASP8*, *TNFα*, and *TP53*, whereas the *BCL-2* mRNA expression after ELF-EMF exposition remained at a comparable level in both groups. Thus, we suggest that increasing the expression of pro-apoptotic genes in post-stroke patients promotes the activation of signaling pathways involved in brain plasticity processes. However, further research is needed to clarify this process.

(E) Ciejka E, Kleniewska P, Skibska B, Goraca A. Effects of extremely low frequency magnetic field on oxidative balance in brain of rats. J Physiol Pharmacol. 62(6):657-661, 2011. (AS, CE, OX)

Extremely low frequency magnetic field (ELF-MF) may result in oxidative DNA damage and lipid peroxidation with an ultimate effect on a number of systemic disturbances and cell death. The aim of the study is to assess the effect of ELF-MF parameters most frequently used in magnetotherapy on reactive oxygen species generation (ROS) in brain tissue of experimental animals depending on the time of exposure to this field. The research material included adult male Sprague-Dawley rats, aged 3-4 months. The animals were divided into 3 groups: I - control (shame) group; II - exposed to the following parameters of the magnetic field: 7 mT, 40 Hz, 30 min/day, 10 days; III - exposed to the ELF-MF parameters of 7 mT, 40 Hz, 60 min/day, 10 days. The selected parameters of oxidative stress: thiobarbituric acid reactive substances (TBARS), hydrogen peroxide (H(2)O(2)), total free sulphydryl groups (-SH groups) and protein in brain homogenates were measured after the exposure of rats to the magnetic field. ELF-MF parameters of 7 mT, 40 Hz, 30 min/day for 10 days caused a significant increase in lipid peroxidation and insignificant increase in H(2)O(2) and free -SH groups. The same ELF-MF parameters but applied for 60 min/day caused a significant increase in free -SH groups and protein concentration in the brain homogenates indicating the adaptive mechanism. The study has shown that ELF-MF applied for 30 min/day for 10 days can affect free radical generation in the brain. Prolongation of the exposure to ELF-MF (60/min/day) caused adaptation to this field. The effect of ELF-MF irradiation on oxidative stress parameters depends on the time of animal exposure to magnetic field.

(E) Clarke D, Penrose MA, Penstone T, Fuller-Carter PI, Hool LC , Harvey AR, Rodger J, Bates KA. Frequency-specific effects of repetitive magnetic stimulation on primary astrocyte cultures. Restor Neurol Neurosci. 35(6):557-569, 2017. (CS, AE, FC)

BACKGROUND: Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive technique that uses magnetic pulses over the cranium to induce electrical currents in underlying cortical tissue. Although rTMS has shown clinical utility for a number of neurological conditions, we have only limited understanding of how rTMS influences cellular function and cell-cell interactions. OBJECTIVE: In this study, we sought to investigate whether repeated magnetic stimulation (rMS) can influence astrocyte biology in vitro. METHOD: We tested four different rMS frequencies and measured the calcium response in primary neonatal astrocyte cultures. We also tested the effect of rMS on astrocyte migration and proliferation in vitro. We tested 3 to 4 culture replicates and 17 to 34 cells for each rMS frequency (sham, 1 Hz, cTBS, 10 Hz and biomemetic high frequency stimulation - BHFS). RESULTS: Of all frequencies tested, 1 Hz stimulation resulted in a statistically significant rise in intracellular calcium in the cytoplasmic and nuclear compartments of the cultured astrocytes. This calcium rise did not affect migration or proliferation in the scratch assay, though astrocyte hypertrophy was reduced in response to 1 Hz rMS, 24 hours post scratch injury. CONCLUSION: Our results provide preliminary evidence that rMS can influence astrocyte physiology,

indicating the potential for a novel mechanism by which rTMS can influence brain activity.

(E)
Colciago A, Audano M, Bonalume V, Melfi V, Mohamed T, Reid AJ, Faroni A, Greer PA, Mitro N, Magnaghi V Transcriptomic Profile Reveals Deregulation of Hearing-Loss Related Genes in Vestibular Schwannoma Cells Following Electromagnetic Field Exposure. Cells 10(7):1840, 2021. (CS, CE, CC, MA)

Hearing loss (HL) is the most common sensory disorder in the world population. One common cause of HL is the presence of vestibular schwannoma (VS), a benign tumor of the VIII cranial nerve, arising from Schwann cell (SC) transformation. In the last decade, the increasing incidence of VS has been correlated to electromagnetic field (EMF) exposure, which might be considered a pathogenic cause of VS development and HL. Here, we explore the molecular mechanisms underlying the biologic changes of human SCs and/or their oncogenic transformation following EMF exposure. Through NGS technology and RNA-Seq transcriptomic analysis, we investigated the genomic profile and the differential display of HL-related genes after chronic EMF. We found that chronic EMF exposure modified the cell proliferation, in parallel with intracellular signaling and metabolic pathways changes, mostly related to translation and mitochondrial activities. Importantly, the expression of HL-related genes such as NEFL, TPRN, OTOGL, GJB2, and REST appeared to be deregulated in chronic EMF exposure. In conclusion, we suggest that, at a preclinical stage, EMF exposure might promote the transformation of VS cells and contribute to HL.

(E) Consales C, Cirotti C, Filomeni G, Panatta M, Butera A, Merla C, Lopresto V, Pinto R, Marino C, Benassi B. Fifty-Hertz Magnetic Field Affects the Epigenetic Modulation of the miR-34b/c in Neuronal Cells. Mol Neurobiol. 55(7):5698-5718, 2018. (CS, AE, OX, CC, ND)

The exposure to extremely low-frequency magnetic fields (ELF-MFs) has been associated to increased risk of neurodegenerative diseases, although the underlying molecular mechanisms are still undefined. Since epigenetic modulation has been recently encountered among the key events leading to neuronal degeneration, we here aimed at assessing if the control of gene expression mediated by miRNAs, namely miRs-34, has any roles in driving neuronal cell response to 50-Hz (1 mT) magnetic field in vitro. We demonstrate that ELF-MFs drive an early reduction of the expression level of miR-34b and miR-34c in SH-SY5Y human neuroblastoma cells, as well as in mouse primary cortical neurons, by affecting the transcription of the common pri-miR-34. This modulation is not p53 dependent, but attributable to the hyper-methylation of the CpG island mapping within the miR-34b/c promoter. Incubation with N-acetyl-l-cysteine or glutathione ethyl-ester fails to restore miR-34b/c expression, suggesting that miRs-34 are not responsive to ELF-MF-induced oxidative stress. By contrast, we show that miRs-34 control reactive oxygen species production and affect mitochondrial oxidative stress triggered by ELF-MFs, likely by modulating mitochondria-related miR-34 targets identified by in silico analysis. We finally demonstrate that ELF-MFs alter the expression of the α-synuclein,

which is specifically stimulated upon ELF-MFs exposure via both direct miR-34 targeting and oxidative stress. Altogether, our data highlight the potential of the ELF-MFs to tune redox homeostasis and epigenetic control of gene expression in vitro and shed light on the possible mechanism(s) producing detrimental effects and predisposing neurons to degeneration.

(E) **Consales C, Merla C, Benassi B, Garcia-Sanchez T, Muscat A, André FM, Marino C, Lluis M Mir LM. Biological effects of ultrashort electric pulses in a Neuroblastoma cell line: the energy density role. Int J Radiat Biol 98(1):109-121, 2022.** (CS, AE, CC)

Background: Despite the numerous literature results about biological effects of electromagnetic field exposure, the interaction mechanisms of these fields with organisms are still a matter of debate. Extremely low frequency magnetic fields can modulate redox homeostasis and we showed that 24 hours exposure to 50 Hz-1 mT has a pro-oxidant effect and effects on the epigenome of SH-SY5Y cells, decreasing miR-34b/c expression through the hypermethylation of their promoter. **Methods:** Here, we investigated the role of the electromagnetic deposited energy density during exposures lasting 24 hours to 1mT amplitude magnetic fields at a frequency of 50 Hz in inducing the above mentioned effects. To this end, we delivered ultrashort electric pulses, in the range of microsecond and nanosecond duration, with the same energy density of the previously performed magnetic exposure to SH-SY5Y cells. Furthermore, we explored the effect of higher deposited energy densities.Analysis of i) gene and microRNA expression, ii) cell morphology, iii) reactive oxygen species (ROS) generation, and iv) apoptosis were carried out.**Results:** We observed significant changes in *egr-1* and *c-fos* expression at very low deposited energy density levels, but no change of the ROS production, miR-34b/c expression, nor the appearance of indicators of apoptosis. We thus sought investigating changes in *egr-1* and *c-fos* expression caused by ultrashort electric pulses at increasing deposited energy density levels. The pulses with the higher deposited energy density caused cell electroporation and even other morphological changes such as cell fusion. The changes in *egr-1* and *c-fos* expression were more intense, but, again, no change of the ROS production, miR-34b/c expression, nor apoptosis induction was observed. **Conclusion:** These results, showing that extremely low levels of electric stimulation (never investigated until now) can cause transcriptional changes, also reveal the safety of the electroporating pulses used in biomedical applications and open up the possibility to further therapeutic applications of this technology.

(E) Cook CM, Saucier DM, Thomas AW, Prato FS. Changes in human EEG alpha activity following exposure to two different pulsed magnetic field sequences. Bioelectromagnetics. 30(1):9-20, 2009. (AE, HU, EE)

The present study investigates the effects of a weak (+/-200 microT(pk)), pulsed, extremely low frequency magnetic field (ELF MF) upon the human electroencephalogram (EEG). We have previously determined that exposure to pulsed ELF MFs can affect the EEG, notably the alpha frequency (8-13 Hz) over the occipital-parietal region of the scalp. In the present study, subjects (n = 32) were exposed to two different pulsed MF sequences (1 and 2, used previously) that differed in presentation rate, in order to examine the effects upon the alpha frequency of the human EEG. Results suggest that compared to sham exposure, alpha activity was lowered over

the occipital-parietal regions of the brain during exposure to Sequence 1, while alpha activity over the same regions was higher after Sequence 2 exposure. These effects occurred after approximately 5 min of pulsed MF exposure. The results also suggest that a previous exposure to the pulsed MF sequence determined subjects' responses in the present experiment. This study supports our previous observation of EEG changes after 5 min pulsed ELF MF exposure. The results of this study are also consistent with existing EEG experiments of ELF MF and mobile phone effects upon the brain.

(E) Corbacio M, Brown S, Dubois S, Goulet D, Prato FS, Thomas AW, Legros A. Human cognitive performance in a 3 mT power-line frequency magnetic field. Bioelectromagnetics. 32(8):620-633, 2011. (HU, AE, BE)

Extremely low frequency (ELF, <300 Hz) magnetic fields (MF) have been reported to modulate cognitive performance in humans. However, little research exists with MF exposures comparable to the highest levels experienced in occupations like power line workers and industrial welders. This research aims to evaluate the impact of a 60 Hz, 3 mT MF on human cognitive performance. Ninety-nine participants completed the double-blind protocol, performing a selection of psychometric tests under two consecutive MF exposure conditions dictated by assignment to one of three groups (sham/sham, MF exposure/sham, or sham/MF exposure). Data were analyzed using a 3 × 2 mixed model analysis of variance. Performance between repetitions improved in 11 of 15 psychometric parameters (practice effect). A significant interaction effect on the digit span forward test ($F = 5.21$, $P < 0.05$) revealed an absence of practice effects for both exposure groups but not the control group. **This memory test indicates MF-induced abolition of the improvement associated with practice**. Overall, this study does not establish any clear MF effect on human cognition. It is speculated that an ELF MF may interfere with the neuropsychological processes responsible for this short-term learning effect supported by brain synaptic plasticity.

(E) Coşkun S, Balabanli B, Canseven A, Seyhan N. Effects of continuous and intermittent magnetic fields on oxidative parameters in vivo. Neurochem Res. 34(2):238-243, 2009. (AS, CE, CC, OX)

Continuous and intermittent 50 Hz, 1.5 mT magnetic field with the exposure period of 4 h/day for 4 days was used to investigate its possible effect on adult guinea pigs. Tissues and plasma specimens were assessed by biochemical parameters. Malondialdehyde (MDA), glutathione (GSH), nitric oxide (NO) levels and myeloperoxidase activity (MPO) were examined in plasma, liver and brain tissues. All parameters were determined by spectrophotometer. While intermittent magnetic field was effective on plasma lipid peroxidation, continuous magnetic field was found to be effective on plasma MPO activity and NO levels. Augmentation of lipid peroxidation was also observed in liver tissue both intermittent and continuous magnetic field exposures. These results indicate that both the intermittent and continuous magnetic field exposures affect various tissues in a distinct manner because of having different tissue antioxidant status and responses.

(E) Cresci A, Durif CMF, Larsen T, Bjelland R, Skiftesvik AB, Browman HI. Magnetic fields produced by subsea high-voltage direct current cables reduce swimming activity of haddock larvae (*Melanogrammus aeglefinus*). PNAS Nexus. 1(4):pgac175, 2022. (AS, CE, BE)

High-voltage direct current (HVDC) subsea cables are used to transport power between locations and from/to nearshore and offshore facilities. HVDC cables produce magnetic fields (B-fields) that could impact marine fish. Atlantic haddock (*Melanogrammus aeglefinus*) is a demersal fish that is at risk of exposure to anthropogenic B-fields. Their larvae drift over the continental shelf, and use the Earth's magnetic field for orientation during dispersal. Therefore, anthropogenic magnetic fields from HVDC cables could alter their behavior. We tested the behavior of 92 haddock larvae using a setup designed to simulate the scenario of larvae drifting past a B-field in the intensity range of that produced by a DC subsea cable. We exposed the larvae to a B-field intensity ranging from 50 to 150 µT in a raceway tank. Exposure to the B-field did not affect the spatial distribution of haddock larvae in the raceway. Larvae were categorized by differences in their exploratory behavior in the raceway. The majority (78%) of larvae were nonexploratory, and exposure to the artificial B-field reduced their median swimming speed by 60% and decreased their median acceleration by 38%. There was no effect on swimming of the smaller proportion (22%) of exploratory larvae. These observations support the conclusion that the swimming performance of nonexploratory haddock larvae would be reduced following exposure to B-field from HVDC cables. The selective impact on nonexploratory individuals, and the lack of impact on exploratory individuals, could have population-scale implications for haddock in the wild.

(E) Cuccurazzu B, Leone L, Podda MV, Piacentini R, Riccardi E, Ripoli C, Azzena GB, Grassi C. Exposure to extremely low-frequency (50 Hz) electromagnetic fields enhances adult hippocampal neurogenesis in C57BL/6 mice. Exp Neurol. 226(1):173-182, 2010. (AS, CE, MC, MA)

Throughout life, new neurons are continuously generated in the hippocampus, which is therefore a major site of structural plasticity in the adult brain. We recently demonstrated that extremely low-frequency electromagnetic fields (ELFEFs) promote the neuronal differentiation of neural stem cells in vitro by up-regulating Ca(v)1-channel activity. The aim of the present study was to determine whether 50-Hz/1 mT ELFEF stimulation also affects adult hippocampal neurogenesis in vivo, and if so, to identify the molecular mechanisms underlying this action and its functional impact on synaptic plasticity. ELFEF exposure (1 to 7 h/day for 7 days) significantly enhanced neurogenesis in the dentate gyrus (DG) of adult mice, as documented by increased numbers of cells double-labeled for 5-bromo-deoxyuridine (BrdU) and double cortin. Quantitative RT-PCR analysis of hippocampal extracts revealed significant ELFEF exposure-induced increases in the transcription of pro-neuronal genes (Mash1, NeuroD2, Hes1) and genes encoding Ca(v)1.2 channel α(1C) subunits. Increased expression of NeuroD1, NeuroD2 and Ca(v)1 channels was also documented by Western blot analysis. Immunofluorescence experiments showed that, 30 days after ELFEF stimulation, roughly half of the newly generated immature neurons had survived and become mature dentate granule cells (as shown by their immunoreactivity for both BrdU and NeuN) and were integrated into the granule cell layer of

the DG. Electrophysiological experiments demonstrated that the new mature neurons influenced hippocampal synaptic plasticity, as reflected by increased long-term potentiation. Our findings show that ELFEF exposure can be an effective tool for increasing in vivo neurogenesis, and they could lead to the development of novel therapeutic approaches in regenerative medicine.

(E) Cui Y, Ge Z, Rizak JD, Zhai C, Zhou Z, Gong S, Che Y. Deficits in water maze performance and oxidative stress in the hippocampus and striatum induced by extremely low frequency magnetic field exposure. PLoS One. 7(5):e32196, 2012. (AS, CE, BE, OX)

The exposures to extremely low frequency magnetic field (ELF-MF) in our environment have dramatically increased. Epidemiological studies suggest that there is a possible association between ELF-MF exposure and increased risks of cardiovascular disease, cancers and neurodegenerative disorders. Animal studies show that ELF-MF exposure may interfere with the activity of brain cells, generate behavioral and cognitive disturbances, and produce deficits in attention, perception and spatial learning. Although, many research efforts have been focused on the interaction between ELF-MF exposure and the central nervous system, the mechanism of interaction is still unknown. In this study, we examined the effects of ELF-MF exposure on learning in mice using two water maze tasks and on some parameters indicative of oxidative stress in the hippocampus and striatum. We found that ELF-MF exposure (1 mT, 50 Hz) induced serious oxidative stress in the hippocampus and striatum and impaired hippocampal-dependent spatial learning and striatum-dependent habit learning. This study provides evidence for the association between the impairment of learning and the oxidative stress in hippocampus and striatum induced by ELF-MF exposure.

(E) Cvetkovic D, Cosic I. Alterations of human electroencephalographic activity caused by multiple extremely low frequency magnetic field exposures. Med Biol Eng Comput. 47(10):1063-1073, 2009. (HU, AE, EE, MA)

In the past, many studies have claimed that extremely low frequency (ELF) magnetic field (MF) exposures could alter the human electroencephalographic (EEG) activity. This study aims at extending our ELF pilot study to investigate whether MF exposures at ELF in series from 50, 16.66, 13, 10, 8.33 to 4 Hz could alter relative power within the corresponding EEG bands. 33 human subjects were tested under a double-blind and counter-balanced conditions. The multiple repeated three-way analysis of variance (ANOVA) mixed design (within and between-subject) analysis was employed followed by post-hoc t-tests and Bonferroni alpha-correction. The results from this study have shown that narrow alpha1 (7.5-9.5 Hz) and alpha2 (9-11 Hz) bands, associated with 8.33 and 10 Hz MF exposures, were significantly ($p < 0.0005$) lower than control over the temporal and parietal regions within the 10-16 min of first MF exposure session and the MF exposures were significantly higher than control of the second session MF exposure (60-65 min from the commencement of testing). Also, it was found that the beta1 (12-14 Hz) band exhibited a significant increase from before to after 13-Hz first MF exposure session at frontal region. The final outcome of our result has shown that it is possible to alter the human EEG activity of alpha and beta bands when exposed to MF at frequencies

corresponding to those same bands, depending on the order and period of MF conditions. This type of EEG synchronisation of driving alpha and beta EEG by alpha and beta sinusoidal MF stimulation, demonstrated in this study, could possibly be applied as therapeutic treatment(s) of particular neurophysiological abnormalities such as sleep and psychiatric disorders.

(E) Das S, Kumar S, Jain S, Avelev VD, Mathur R. Exposure to ELF- magnetic field promotes restoration of sensori-motor functions in adult rats with hemisection of thoracic spinal cord. Electromagn Biol Med. 31(3):180-194, 2012. (AS, CE, ME, BE, MA)

Clinically effective modalities of treatment for spinal cord injury (SCI) still remain unsatisfactory and are largely invasive in nature. There are reports of accelerated regeneration in injured peripheral nerves by extremely low-frequency pulsed electromagnetic field (ELF-EMF) in the rat. In the present study, the effect of (50 Hz), low-intensity (17.96 µT) magnetic field (MF) exposure of rats after-hemisection of T13 spinal cord (hSCI) was investigated on sensori-motor and locomotor functions. Rats were divided into hSCI (sham-exposed) and hSCI+MF (MF: 2 h/d X 6 weeks) groups. Besides their general conditions, locomotor function by Basso, Beattie, and Brenahan (BBB) score; motor responses to noxious stimuli by threshold of tail flick (TTF), simple vocalization (TSV), tail flick latency (TFL), and neuronal excitability by H-reflex were noted. It is found that, in the hSCI+MF group, a statistically significant improvement over the hSCI control group was noted in BBB score from post-SCI wk2 and TFL and TTF by post-hSCI wk1 and wk3, respectively. Correspondingly, TSV gradually restored by post-hSCI wk5.The threshold of H-reflex was reduced on ipsilateral side vs. contralateral side in hSCI and hSCI+MF group. A complete bladder control was dramatically restored on post-hSCI day4 (vs. day7 of hSCI group) and the survival rate was 100% in the hSCI+MF group (vs. 90% of hSCI group). The results of our study suggest that extremely low-frequency (50 Hz), low-intensity (17.96 µT) MF exposure for 2 h/d x 6wks promotes recovery of sensori-motor behavior including locomotion and bladder control both in terms of temporal pattern and magnitude in hemisection injury of (T13) spinal cord rats.

(E) Davanipour Z, Tseng C-C, Lee PJ, Markides KS, Sobel E. Severe Cognitive Dysfunction and Occupational Extremely Low Frequency Magnetic Field Exposure among Elderly Mexican Americans. Brit J Med Med Res 4 (8): 1641-1662, 2014. (HU, BE)

Aims: This report is the first study of the possible relationship between extremely low frequency (50-60 Hz, ELF) magnetic field (MF) exposure and severe cognitive dysfunction. Earlier studies investigated the relationships between MF occupational exposure and Alzheimer's disease (AD) or dementia. These studies had mixed results, depending upon whether the diagnosis of AD or dementia was performed by experts and upon the methodology used to classify MF exposure. Study Design: Population-based case-control. Place and Duration of Study: Neurology and Preventive Medicine, Keck School of Medicine, University of Southern California, 2 years. Methodology: The study population consisted of 3050 Mexican Americans, aged 65+, enrolled in Phase 1 of the Hispanic Established Population for the Epidemiologic Study of the Elderly (H-EPESE) study. Mini-Mental State Exam (MMSE) results, primary occupational history, and other data were collected. Severe cognitive dysfunction was defined

as an MMSE score below 10. The MF exposure methodology developed and used in earlier studies was used. Results: Univariate odds ratios (OR) were 3.4 (P< .03; 95% CI: 1.3-8.9) for high and 1.7 (P=.27; 95% CI: 0.7-4.1) for medium or high (M/H) MF occupations. In multivariate main effects models, the results were similar. When interaction terms were allowed in the models, the interactions between M/H or high occupational MF exposure and smoking history or age group were statistically significant, depending upon whether two (65-74, 75+) or three (65-74, 75-84, 85+) age groups were considered, respectively. When the analyses were limited to subjects aged 75+, the interactions between M/H or high MF occupations and a positive smoking history were statistically significant. Conclusion: The results of this study indicate that working in an occupation with high or M/H MF exposure may increase the risk of severe cognitive dysfunction. Smoking and older age may increase the deleterious effect of MF exposure.

(E) Davarpanah Jazi S, Modolo J, Baker C, Villard S, Legros A. Effects of A 60 Hz Magnetic Field of Up to 50 milliTesla on Human Tremor and EEG: A Pilot Study. Int J Environ Res Public Health. 14(12):1446, 2017. (HU, AE, EE)

Humans are surrounded by sources of daily exposure to power-frequency (60 Hz in North America) magnetic fields (MFs). Such time-varying MFs induce electric fields and currents in living structures which possibly lead to biological effects. The present pilot study examined possible extremely low frequency (ELF) MF effects on human neuromotor control in general, and physiological postural tremor and electroencephalography (EEG) in particular. Since the EEG cortical mu-rhythm (8-12 Hz) from the primary motor cortex and physiological tremor are related, it was hypothesized that a 60 Hz MF exposure focused on this cortical region could acutely modulate human physiological tremor. Ten healthy volunteers (age: 23.8 ± 4 SD) were fitted with a MRI-compatible EEG cap while exposed to 11 MF conditions (60 Hz, 0 to 50 mT_{rms}, 5 mT_{rms} increments). Simultaneously, physiological tremor (recorded from the contralateral index finger) and EEG (from associated motor and somatosensory brain regions) were measured. Results showed no significant main effect of MF exposure conditions on any of the analyzed physiological tremor characteristics. In terms of EEG, no significant effects of the MF were observed for C1, C3, C5 and CP1 electrodes. However, a significant main effect was found for CP3 and CP5 electrodes, both suggesting a decreased mu-rhythm spectral power with increasing MF flux density. This is however not confirmed by Bonferroni corrected pairwise comparisons. Considering both EEG and tremor findings, no effect of the MF exposure on human motor control was observed. However, MF exposure had a subtle effect on the mu-rhythm amplitude in the brain region involved in tactile perception. Current findings are to be considered with caution due to the small size of this pilot work, but they provide preliminary insights to international agencies establishing guidelines regarding electromagnetic field exposure with new experimental data acquired in humans exposed to high mT-range MFs.

(E) de Kleijn S, G. Ferwerda, M. Wiese, J. Trentelman, J. Cuppen, T Kozicz, L. de Jager, PWM Hermans, BML Verburg-van Kemenade. A short-term extremely low

frequency electromagnetic field exposure increases circulating leukocyte numbers and affects HPA-axis signaling in mice Bioelectromagnetics 37(7):433-443, 2016.(AS, CE, CC) Free PMC article

There is still uncertainty whether extremely low frequency electromagnetic fields (ELF-EMF) can induce health effects like immunomodulation. Despite evidence obtained in vitro, an unambiguous association has not yet been established in vivo. Here, mice were exposed to ELF-EMF for 1, 4, and 24 h/day in a short-term (1 week) and long-term (15 weeks) set-up to investigate whole body effects on the level of stress regulation and immune response. ELF-EMF signal contained multiple frequencies (20-5000 Hz) and a magnetic flux density of 10 µT. After exposure, blood was analyzed for leukocyte numbers (short-term and long-term) and adrenocorticotropic hormone concentration (short-term only). Furthermore, in the short-term experiment, stress-related parameters, corticotropin-releasing hormone, proopiomelanocortin (POMC) and CYP11A1 gene-expression, respectively, were determined in the hypothalamic paraventricular nucleus, pituitary, and adrenal glands. In the short-term but not long-term experiment, leukocyte counts were significantly higher in the 24 h-exposed group compared with controls, mainly represented by increased neutrophils and CD4 ± lymphocytes. POMC expression and plasma adrenocorticotropic hormone were significantly lower compared with unexposed control mice. In conclusion, short-term ELF-EMF exposure may affect hypothalamic-pituitary-adrenal axis activation in mice. Changes in stress hormone release may explain changes in circulating leukocyte numbers and composition.

(NE) de Groot MW, Kock MD, Westerink RH. Assessment of the neurotoxic potential of exposure to 50Hz extremely low frequency electromagnetic fields (ELF-EMF) in naïve and chemically-stressed PC12 cells. Neurotoxicology. 44:358-364, 2014. (CS, AE, CC, OX)

Increasing exposure to extremely low frequency electromagnetic fields (ELF-EMF), generated by power lines and electric appliances, raises concern about potential adverse health effects of ELF-EMF. The central nervous system is expected to be particularly vulnerable to ELF-EMF as its function strongly depends on electrical excitability. We therefore investigated effects of acute (30min) and sub-chronic (48h) exposure to 50Hz ELF-EMF on naïve and chemically-stressed pheochromocytoma (PC12) cells. The latter have higher levels of iron and/or reactive oxygen species (ROS) and display increased vulnerability to environmental insults. Effects of ELF-EMF on Ca^{2+}-homeostasis, ROS production and membrane integrity were assessed using Fura-2 single cell fluorescence microscopy, H_2-DCFDA and CFDA assays, respectively. Our data demonstrate that acute exposure of naïve PC12 cells to 50 Hz ELF-EMF up to 1000 µT fails to affect basal or depolarization-evoked $[Ca^{2+}]_i$. Moreover, sub-chronic ELF-EMF exposure up to 1000µT has no consistent effects on Ca^{2+}-homeostasis in naïve PC12 cells and does not affect ROS production and membrane integrity. Notably, in chemically-stressed PC12 cells both acute and sub-chronic ELF-EMF exposure also failed to exert consistent effects on Ca^{2+}-homeostasis, ROS production and membrane integrity. Our combined findings thus indicate that exposure to 50Hz ELF-EMF up to 1000 µT, i.e. 10,000 times above background exposure, does not induce neurotoxic effects in vitro, neither in naïve nor in chemically-stressed PC12 cells. Though our data require confirmation, e.g. in developing neuronal cells in vitro or (developing) animals, it appears that the neurotoxic risk of ELF-EMF exposure is limited.

(E) de Groot MW, van Kleef RG, de Groot A, Westerink RH. In vitro developmental neurotoxicity following chronic exposure to 50 Hz extremely low frequency electromagnetic fields (ELF-EMF) in primary rat cortical cultures. Toxicol Sci. 149:433-440, 2016. (CS, CE, CC)

Exposure to 50-60 Hz extremely low frequency electromagnetic fields (ELF-EMFs) has increased considerably over the last decades. Several epidemiological studies suggested that ELF-EMF exposure is associated with adverse health effects, including neurotoxicity. However, these studies are debated as results are often contradictory and the possible underlying mechanisms are unknown. Since the developing nervous system is particularly vulnerable to insults, we investigate effects of chronic, developmental ELF-EMF exposure in vitro. Primary rat cortical neurons received 7 days developmental exposure to 50 Hz block-pulsed ELF-EMF (0-1000 µT) to assess effects on cell viability (Alamar Blue/CFDA assay), calcium homeostasis (single cell fluorescence microscopy), neurite outgrowth (β(III)-Tubulin immunofluorescent staining) and spontaneous neuronal activity (multi-electrode arrays [MEAs]). Our data demonstrate that cell viability is not affected by developmental ELF-EMF (0-1000 µT) exposure. Depolarization- and glutamate-evoked increases in intracellular calcium concentration ([Ca2+]i) are slightly increased at 1 µT, whereas both basal and stimulation-evoked [Ca2+]i show a modest inhibition at 1000 µT. Subsequent morphological analysis indicated that neurite length is unaffected up to 100 µT, but increased at 1000 µT. However, neuronal activity appeared largely unaltered following chronic ELF-EMF exposure up to 1000 µT. The effects of ELF-EMF exposure were small and largely restricted to the highest field strength (1000 µT), i.e. 10,000 times above background exposure and well above current residential exposure limits. Our combined data therefore indicate that chronic ELF-EMF exposure has only limited (developmental) neurotoxic potential in vitro.

(E) Del Giudice E, Facchinetti F, Nofrate V, Boccaccio P, Minelli T, Dam M, Leon A, Moschini G. Fifty Hertz electromagnetic field exposure stimulates secretion of beta-amyloid peptide in cultured human neuroglioma. Neurosci Lett. 418(1):9-12, 2007. (CS, CE, ND)

Recent epidemiological studies raise the possibility that individuals with occupational exposure to low frequency (50-60 Hz) electromagnetic fields (LF-EMF), are at increased risk of Alzheimer's disease (AD). However, the mechanisms through which LF-EMF may affect AD pathology are unknown. We here tested the hypothesis that the exposure to LF-EMF may affect amyloidogenic processes. We examined the effect of exposure to 3.1 mT 50 Hz LF-EMF on Abeta secretion in H4 neuroglioma cells stably overexpressing human mutant amyloid precursor protein. We found that overnight exposure to LF-EMF induces a significant increase of amyloid-beta peptide (Abeta) secretion, including the isoform Abeta 1-42, without affecting cell survival. These findings show for the first time that exposure to LF-EMF stimulates Abeta secretion in vitro, thus alluding to a potential link between LF-EMF exposure and APP processing in the brain.

(E) Deng Y, Zhang Y, Jia S, Liu J, Liu Y, Xu W, Liu L. Effects of aluminum and extremely low frequency electromagnetic radiation on oxidative stress and memory in brain of mice. Biol Trace Elem Res. 156(1-3):243-252, 2013. (AS, CE, BE, OX)

This study was aimed to investigate the effect of aluminum and extremely low-frequency magnetic fields (ELF-MF) on oxidative stress and memory of SPF Kunming mice. Sixty male SPF Kunming mice were divided randomly into four groups: control group, ELF-MF group (2 mT, 4 h/day), load aluminum group (200 mg aluminum/kg, 0.1 ml/10 g), and ELF-MF + aluminum group (2 mT, 4 h/day, 200 mg aluminum/kg). After 8 weeks of treatment, the mice of three experiment groups (ELF-MF group, load aluminum group, and ELF-MF + aluminum group) exhibited firstly the learning memory impairment, appearing that the escaping latency to the platform was prolonged and percentage in the platform quadrant was reduced in the Morris water maze (MWM) task. Secondly are the pathologic abnormalities including neuronal cell loss and overexpression of phosphorylated tau protein in the hippocampus and cerebral cortex. On the other hand, the markers of oxidative stress were determined in mice brain and serum. The results showed a statistically significant decrease in superoxide dismutase activity and increase in the levels of malondialdehyde in the ELF-MF group ($P < 0.05$ or $P < 0.01$), load aluminum group ($P < 0.01$), and ELF-MF + aluminum group ($P < 0.01$). However, the treatment with ELF-MF + aluminum induced no more damage than ELF-MF and aluminum did, respectively. In conclusion, both aluminum and ELF-MF could impact on learning memory and pro-oxidative function in Kunming mice. However, there was no evidence of any association between ELF-MF exposure with aluminum loading.

(E) Dey S, Bose S, Kumar S, Rathore R, Mathur R, Jain S. Extremely low frequency magnetic field protects injured spinal cord from the microglia- and iron-induced tissue damage. Electromagn Biol Med. 36:330-340, 2017. (AS, CE, FC, MA)

Spinal cord injury (SCI) is insult to the spinal cord, which results in loss of sensory and motor function below the level of injury. SCI results in both immediate mechanical damage and secondary tissue degeneration. Following traumatic insult, activated microglia release proinflammatory cytokines and excess iron due to hemorrhage, initiating oxidative stress that contributes to secondary degeneration. Literature suggests that benefits are visible with the reduction in concentration of iron and activated microglia in SCI. Magnetic field attenuates oxidative stress and promotes axonal regeneration in vitro and in vivo. The present study demonstrates the potential of extremely low frequency magnetic field to attenuate microglia- and iron-induced secondary injury in SCI rats. Complete transection of the spinal cord (T13 level) was performed in male Wistar rats and subsequently exposed to magnetic field (50 Hz,17.96 μT) for 2 h daily for 8 weeks. At the end of the study period, spinal cords were dissected to quantify microglia, macrophage, iron content and study the architecture of lesion site. A significant improvement in locomotion was observed in rats of the SCI + MF group as compared to those in the SCI group. Histology, immunohistochemistry and flow cytometry revealed significant reduction in lesion volume, microglia, macrophage, collagen tissue and iron content, whereas, a significantly higher vascular endothelial

growth factor expression around the epicenter of the lesion in SCI + MF group as compared to SCI group. These novel findings suggest that exposure to ELF-MF reduces lesion volume, inflammation and iron content in addition to facilitation of angiogenesis following SCI.

(E) Di G, Kim H, Xu Y, Kim J, Gu X. A comparative study on influences of static electric field and power frequency electric field on cognition in mice. Environ Toxicol Pharmacol. 66:91-95, 2019. (AS, CE, BE, EE)

Recently, electromagnetic fields around ultra-high voltage transmission lines have received considerable attentions for their potential biological effects. This study aimed to investigate the effects of static electric field (SEF) and power frequency electric field (PFEF) on cognition. Mice were exposed to SEF and PFEF with the same strength (35 kV/m) for 49 days, respectively. Behaviors in Morris water maze test and amino acid neurotransmitter levels in hippocampus were examined during exposure. Results indicated that the exposure of 35 kV/m SEF would not cause significant influences on learning and memory ability in mice, while the exposure of 35 kV/m PFEF would cause significant positive effects on learning and memory ability in mice on day 33. This difference in effects from SEF and PFEF on cognition was possibly induced by the difference in the degree of molecular polarization and ion migration in organisms under exposure of two kinds of electric fields with different frequency.

(E) Di Loreto S, Falone S, Caracciolo V, Sebastiani P, D'Alessandro A, Mirabilio A, Zimmitti V, Amicarelli F. Fifty hertz extremely low-frequency magnetic field exposure elicits redox and trophic response in rat-cortical neurons. J Cell Physiol. 219(2):334-343, 2009. (CS, AE, CC, OX)

Large research activity has raised around the mechanisms of interaction between extremely low-frequency magnetic fields (ELF-MFs) and biological systems. ELF-MFs may interfere with chemical reactions involving reactive oxygen species (ROS), thus facilitating oxidative damages in living cells. Cortical neurons are particularly susceptible to oxidative stressors and are also highly dependent on the specific factors and proteins governing neuronal development, activity and survival. The aim of the present work was to investigate the effects of exposures to two different 50 Hz sinusoidal ELF-MFs intensities (0.1 and 1 mT) in maturing rat cortical neurons' major anti-oxidative enzymatic and non-enzymatic cellular protection systems, membrane peroxidative damage, as well as growth factor, and cytokine expression pattern. Briefly, our results showed that ELF-MFs affected positively the cell viability and concomitantly reduced the levels of apoptotic death in rat neuronal primary cultures, with no significant effects on the main anti-oxidative defences. Interestingly, linear regression analysis suggested a positive correlation between reduced glutathione (GSH) and ROS levels in 1 mT MF-exposed cells. On this basis, our hypothesis is that GSH could play an important role in the antioxidant defence towards the ELF-MF-induced redox challenge. Moreover, the GSH-based cellular response was achieved together with a brain-derived neurotrophic factor over-expression as well as with the interleukin 1beta-dependent regulation of pro-survival signaling pathways after ELF-MF exposure.

(E) Dileone M, Carrasco-López MC, Segundo-Rodriguez JC, Mordillo-Mateos L, López-Ariztegui N, Alonso-Frech F, Catalan-Alonso MJ, Obeso JA, Oliviero A, Foffani G, Dopamine-dependent changes of cortical excitability induced by transcranial static magnetic field stimulation in Parkinson's disease. Sci Rep. 7(1):4329, 2017. (HU, AE, ND, CE, EE, MA)

Transcranial static magnetic field stimulation (tSMS) is a recent low-cost non-invasive brain stimulation technique that decreases cortical excitability in healthy subjects. The objective of the present study was to test the ability of tSMS to modulate cortical excitability in patients with Parkinson's disease. We performed a randomized double-blind sham-controlled cross-over study to assess cortical excitability before and immediately after tSMS (or sham) applied for 10 min to the more affected motor cortex of patients with Parkinson's disease. Cortical excitability was quantified by the amplitude of motor evoked potentials (MEPs) elicited by single-pulse transcranial magnetic stimulation (TMS). tSMS significantly decreased MEP amplitudes in patients OFF medication (after overnight withdrawal of dopaminergic drugs), but not ON medication (after an acute dose of levodopa). The between-patients variability of tSMS-induced changes was significantly greater ON medication. The variability ON medication could be partly explained by disease progression, i.e. the more advanced the patient, the more likely it was to observe a switch from inhibitory tSMS plasticity OFF medication to paradoxical facilitatory plasticity ON medication. These results suggest that tSMS induces dopamine-dependent changes of cortical excitability in patients with Parkinson's disease.

(E) Dileone M, Mordillo-Mateos L, Oliviero A, Foffani G. Long-lasting effects of transcranial static magnetic field stimulation on motor cortex excitability. Brain Stimul. 11(4):676-688, 2018. (HU, AE, EE)

BACKGROUND: Transcranial static magnetic field stimulation (tSMS) was recently added to the family of inhibitory non-invasive brain stimulation techniques. However, the application of tSMS for 10-20 min over the motor cortex (M1) induces only short-lasting effects that revert within few minutes. OBJECTIVE: We examined whether increasing the duration of tSMS to 30 min leads to long-lasting changes in cortical excitability, which is critical for translating tSMS toward clinical applications. METHODS: The study comprised 5 experiments in 45 healthy subjects. We assessed the impact of 30-min-tSMS over M1 on corticospinal excitability, as measured by the amplitude of motor evoked potentials (MEPs) and resting motor thresholds (RMTs) to single-pulse transcranial magnetic stimulation (TMS) (experiments 1-2). We then assessed the impact of 30-min-tSMS on intracortical excitability, as measured by short-interval intracortical facilitation (SICF) and short-interval intracortical inhibition (SICI) using paired-pulse TMS protocols (experiments 2-4). We finally assessed the impact of 10-min-tSMS on SICF and SICI (experiment 5). RESULTS: 30-min-tSMS decreased MEP amplitude compared to sham for at least 30 min after the end of the stimulation. This long-lasting effect was associated with increased SICF and reduced SICI. 10-min-tSMS -previously reported to induce a short-lasting decrease in MEP amplitude- produced the opposite changes in intracortical excitability, decreasing SICF while increasing SICI. CONCLUSIONS: <u>These results suggest a dissociation of intracortical</u>

changes in the consolidation from short-lasting to long-lasting decrease of corticospinal excitability induced by tSMS. The long-lasting effects of 30-min-tSMS open the way to the translation of this simple, portable and low-cost technique toward clinical trials.

(E) Dimitrijević D, Savić T, Anđelković M, Prolić Z, Janać B. Extremely low frequency magnetic field (50 Hz, 0.5 mT) modifies fitness components and locomotor activity of Drosophila subobscura. Int J Radiat Biol. 90:337-343, 2014. (AS, AE, DE, BE)

Purpose: Extremely low frequency (ELF) magnetic fields are essential ecological factor which may induce changes in many organisms. The aim of this study was to examine the effects in Drosophila subobscura exposed for 48 h to ELF magnetic field (50 Hz, 0.5 mT) at different developmental stages. Materials and methods: Egg-first instar larvae developmental stage of D. subobscura isofemale lines was exposed to ELF magnetic field, and fitness components (developmental time, developmental dynamics, viability and sex ratio) and locomotor activity of 3-days old males and females were monitored. Also, just eclosed D. subobscura isofemale adults were exposed to ELF magnetic field and their locomotor activity was monitored just after. Results: ELF magnetic field shortens developmental time, increases viability and does not affect sex ratio of D. subobscura. No matter which developmental stage is exposed, ELF magnetic field significantly decreases locomotor activity of adult flies, but after exposure of just eclosed adults observed change lasts longer. Conclusions: Applied ELF magnetic field modifies fitness components and locomotor activity of D. subobscura. Observed effects can be attributed to the influence of magnetic field on different stages of development where the hormonal and nervous systems play important role in the control of examined parameters.

(E) Dinčić M, Krstić DZ, Čolović MB, Nešović Ostojić J, Kovačević S, De Luka SR, Djordjević DM, Ćirković S, Brkić P, Todorović J. Modulation of rat synaptosomal ATPases and acetylcholinesterase activities induced by chronic exposure to the static magnetic field. Int J Radiat Biol. 94(11):1062-1071, 2018. (AS, CE, OX, CC, MA)

PURPOSE: It is considered that exposure to static magnetic fields (SMF) may have both detrimental and therapeutic effect, but the mechanism of SMF influence on the living organisms is not well understood. Since the adenosine triphosphatases (ATPases) and acetylcholinesterase (AChE) are involved in both physiological and pathological processes, the modulation of Na^+/K^+-ATPase, ecto-ATPases and AChE activities, as well as oxidative stress responses were followed in synaptosomes isolated from rats after chronic exposure toward differently oriented SMF. MATERIAL AND METHODS: Wistar albino rats were randomly divided into three experimental groups (six animals per group): Up and Down group - exposed to upward and downward oriented SMF, respectively, and Control group. After 50 days, the rats were sacrificed, and synaptosomes were isolated from the whole rat brain and used for testing the enzyme activities and oxidative stress parameters. RESULTS: Chronic exposure to 1 mT SMF significantly increased ATPases, AChE activities, and malondialdehyde (MDA) level in both exposed groups, compared to control values. The significant

decrease in synaptosomal catalase activity (1.48 ± 0.17 U/mg protein) induced by exposure to the downward oriented field, compared to those obtained for Control group (2.60 ± 0.29 U/mg protein), and Up group (2.72 ± 0.21 U/mg protein). CONCLUSIONS: It could be concluded that chronic exposure to differently oriented SMF increases ATPases and AChE activities in rat synaptosomes. Since brain ATPases and AChE have important roles in the pathogenesis of several neurological diseases, SMF influence on the activity of these enzymes may have potential therapeutic importance.

(E) Ding H-M, Wang X, Mo W-C, Qin L-L, Wong S, Fu J-P, Tan Y, Liu Y, He R-Q, Hua Q. Hypomagnetic fields cause anxiety in adult male mice. Bioelectromagnetics 40(1):27-32, 2019. (AS, AE, BE)

Hypomagnetic fields (HMF), that is, the elimination of the geomagnetic field (GMF), are a risk factor to the health of astronauts in outer space. It has been established that continuous HMF exposure affects cytoskeleton assembly, cell proliferation, embryonic development, and even learning and memory. In addition, although there were some previous studies that focused on the effects of long-term HMF-exposure, so far very limited investigations have been conducted to examine the short-term HMF effect in animals. In this study, we exposed adult male C57BL/6 mice to a 3-axis Helmholtz-coil HMF-simulation system for 72 h and found that short-term HMF-exposure induced a significant increase in anxiety-related behaviors. And our findings provide important information for both psychological intervention and the health care of astronauts.

(E) Djordjevic NZ, Paunović MG, Peulić AS. Anxiety-like behavioural effects of extremely low-frequency electromagnetic field in rats. Environ Sci Pollut Res Int. 24(27):21693-21699, 2017. (AS, CE, BE, OX)

In recent years, extremely low-frequency electromagnetic field (ELF-EMF) has received considerable attention for its potential biological effects. Numerous studies have shown the role of ELF-EMF in behaviour modulation. The aim of this study was to investigate the effect of short-term ELF-EMF (50 Hz) in the development of anxiety-like behaviour in rats through change hypothalamic oxidative stress and NO. Ten adult male rats (Wistar albino) were divided in two groups: control group-without exposure to ELF-EMF and experimental group-exposed to ELF-EMF during 7 days. After the exposure, time open field test and elevated plus maze were used to evaluate the anxiety-like behaviour of rats. Upon completion of the behavioural tests, concentrations of superoxide anion ($O_2^{\cdot -}$), nitrite (NO_2^-, as an indicator of NO) and peroxynitrite ($ONOO^-$) were determined in the hypothalamus of the animals. Obtained results show that ELF-EMF both induces anxiety-like behaviour and increases concentrations of $O_2^{\cdot -}$ and NO, whereas it did not effect on $ONOO^-$ concentration in hypothalamus of rats. In conclusion, the development of anxiety-like behaviour is mediated by oxidative stress and increased NO concentration in hypothalamus of rats exposed to ELF-EMF during 7 days.

(E) Dong L, Zheng Y, Li ZY, Li G, Lin L. Modulating effects of on-line low frequency electromagnetic fields on hippocampal long-term potentiation in young male Sprague-Dawley rat. J Neurosci Res. 96(11):1775-1785, 2018. (CS, AE, EE)

The low frequency electromagnetic fields (LF-EMFs) are attracting more attention and studied deeply because of their effects on human health and biology. Recent reports indicate that exposure of rats to LF-EMFs induces persistent changes in neuronal activity. The studies used the following standard methods: the rats or rat brain slices were first stimulated in an external electromagnetic exposure system, and then moved to a patch clamp perfusion chamber to record electrophysiological characteristics (off-line magnetic exposure). However, this approach is susceptible to many disturbances, such as the effects of brain slice movements. In this paper, we describe a novel patch-clamp setup which is modified to allow accurate on-line LF-EMFs stimulation. We performed the computational simulations of the stimulation coils to describe the uniformity of the distribution of the on-line magnetic field. The 0.5, 1, 2 mT magnetic field of 15 Hz, 50 Hz, and 100 Hz was produced and applied to slices to study the effect of LF-EMFs on synaptic plasticity. We demonstrated that the slope of field excitatory postsynaptic potentials (fEPSPs) decreased significantly under the priming on-line uninterrupted or pulsed sinusoidal LF-EMFs stimulation. In the present study, we investigated whether LF-EMFs can induce long-term potentiation (LTP) in male Sprague-Dawley rat hippocampal slices in vitro. Interestingly, these results highlight the role of 100 Hz pulsed sinusoidal LF-EMFs only as a modulator, rather than an LTP inducer.

(E) Duan Y, Wang Z, Zhang H, He Y, Lu R, Zhang R, Sun G, Sun X. The preventive effect of lotus seedpod procyanidins on cognitive impairment and oxidative damage induced by extremely low frequency electromagnetic field exposure. Food Funct. 4(8):1252-1262, 2013. (AS, CE, BE, OX)

The present study investigated the effects of lotus seedpod procyanidins (LSPCs) administered by oral gavage on the cognitive deficits and oxidative damage of mice at extremely low frequency electromagnetic field (ELF-EMF) exposure (50 Hz, 8 mT, 28 days). The results showed that 90 mg kg^{-1} LSPCs treatment significantly increased body weight compared with the ELF-EMF group at ELF-EMF exposure and effectively maintained liver index, thymus index, kidney index and spleen index close to normal. A water maze test indicated that learning and memory abilities of the ELF-EMF group deteriorated significantly with ELF-EMF exposure when compared with the control group, but the ELF-EMF + LSPCs90 group had remarkably improved learning and memory abilities compared with the ELF-EMF group. Malondialdehyde (MDA), reactive oxygen species (ROS), nitric oxide (NO) and nitric oxide synthase (NOS) mostly exhibited significant increases, while the activities of glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD) decreased significantly under ELF-EMF exposure in the ELF-EMF group. LSPCs (especially 60, 90 mg kg^{-1}) administration decreased MDA, ROS, NO content and lowered NOS activity in LSPCs treatment groups. Furthermore, LSPCs (60, 90 mg kg^{-1}) treatment significantly augmented GPx, CAT, SOD activity in the hippocampus and serum. Pathological observation showed that number of pyramidal cells of the CA1 and CA3 regions of the hippocampus of the LSPCs treatment groups was significantly greater than the ELF-EMF group. All the data suggested that the LSPCs can effectively prevent learning and memory

damage and oxidative damage caused by the ELF-EMF, most likely through the ability of LSPCs to scavenge oxygen free radicals and to stimulate antioxidant enzyme activity.

(E) Duan Y, Wang Z, Zhang H, He Y, Fan R, Cheng Y, Sun G, Sun X. Extremely low frequency electromagnetic field exposure causes cognitive impairment associated with alteration of the glutamate level, MAPK pathway activation and decreased CREB phosphorylation in mice hippocampus: reversal by procyanidins extracted from the lotus seedpod. Food Funct. 5(9):2289-2297, 2014. (AS, CE, FC, CC)

Lotus seedpod procyanidins (LSPCs) could effectively prevent learning and memory damage and oxidative damage caused by extremely low frequency electromagnetic field (ELF-EMF) exposure. However, LSPCs protect neurons from ELF-EMF-induced damage by mechanisms currently not clear. An excessive release of glutamate is considered to be one of the molecular mechanisms of neuronal damage in several neurological diseases. In this study we determined whether the ELF-EMF (50 Hz, 8 mT, 28 days) exposure induced alterations of glutamate release in mice hippocampus and explored the possible mechanism, and if LSPC treatment normalized its alterations. The results showed that ELF-EMF exposure induced the increased contents of glutamate, GABA, excessively activated NMDA receptors, increasing the number of NMDA receptor 2B (NR2B) and intracellular Ca^{2+} concentration $[Ca^{2+}]_i$ in hippocampus. In addition, ELF-EMF exposure decreased the ERK1/2 and CREB phosphorylation, which suggested that the Ca^{2+} influx induced by the ELF-EMF exposure stimulated activity of the ERK, in turn, influences the expression of downstream proteins in this signaling pathway. Besides, ELF-EMF exposure also increased JNK1/2 phosphorylation through the activated ASK1, which plays a pivotal role in hippocampal neuronal cell death. However, oral administration of LSPCs (especially 60 and 90 mg kg^{-1}) markedly improved expressions of p-CREB, p-ERK1/2 and p-JNK1/2, accompanied by decreased levels of glutamate, GABA, $[Ca^{2+}]_i$ and NR2B. Thus, the results from the present study suggest that p-ERK1/2, p-JNK1/2, $[Ca^{2+}]_i$ and p-CREB expression normalized, possibly via a NMDA receptor-channel through the changes of GABA, glutamate and NR2B, which might be responsible for the neuroprotective or memory enhancing effects of LSPCs.

(E) Durif CMF, Nyqvist D, Taormina B, Shema SD, Skiftesvik AB, Freytet F, Browman HI. Magnetic fields generated by submarine power cables have a negligible effect on the swimming behavior of Atlantic lumpfish (*Cyclopterus lumpus*) juveniles. PeerJ. 11:e14745, 2023. (AS, CE, BE)

Submarine power cables carry electricity over long distances. Their geographic distribution, number, and areal coverage are increasing rapidly with the development of, for example, offshore wind facilities. The flow of current passing through these cables creates a magnetic field (MF) that can potentially affect marine organisms, particularly those that are magnetosensitive. The lumpfish (*Cyclopterus lumpus*) is a migratory species that is widely distributed in the North Atlantic Ocean and Barents Sea. It migrates between coastal spawning grounds and pelagic offshore feeding areas. We tested whether lumpfish respond to MFs of the same intensity as those emitted by high voltage direct current (HVDC) submarine power cables. Laboratory experiments were conducted by placing juvenile lumpfish in an artificial MF gradient generated by a Helmholtz coil system. The intensity of the artificial MF used (230 µT) corresponded to the

field at 1 m from a high-power submarine cable. The fish were filmed for 30 min with the coil either on or off. Swimming speeds, and presence in the different parts of a raceway, were extracted from the videos and analyzed. Juvenile lumpfish activity, defined as the time that the fish spent swimming relative to stationary pauses (attached to the substrate), and the distance travelled, were unaffected by exposure to the artificial MF. The swimming speed of juvenile lumpfish was reduced (by 16%) when the coil was on indicating that the fish could either sense the MF or the induced electric field created by the movement of the fish through the magnetic field. However, it seems unlikely that a 16% decrease in swimming speed occurring within 1 m of HVDC cables would significantly affect Atlantic lumpfish migration or homing.

(E) Eduardo PI, Leticia VD. High-frequency transcranial magnetic stimulation decreases dorsal striatum dopamine D2 receptors in a rat model of depression. Brain Res. 2025 Nov 4:150016. doi: 10.1016/j.brainres.2025.150016. Epub ahead of print. (AS, CE, CC, BE, MA)

Major Depressive Disorder (MDD) is a prevalent chronic mental illness worldwide. Antidepressants are a fundamental part of their treatment, being effective in 60-70 % of patients. Alternative therapies, such as repetitive transcranial magnetic stimulation (rTMS), have also been proposed for modulating cortical neuronal activity and activating circuits associated with the stimulated area. Dopamine is one of the principal neurotransmitters in the nigrostriatal pathway. Changes in dopaminergic transmission through the mesolimbic pathway have been identified as part of the pathophysiology of depression; however, there are only a small number of studies examining the relationship between the nigrostriatal pathway and depression. This study aims to describe the effect of rTMS on the dorsal striatum and prefrontal cortex in a rat model of depression. Behaviors associated with the developed depression and anxiety were assessed through a test battery consisting of sucrose preference, forced swimming, open field, and elevated plus maze. The10 Hz rTMS was applied daily for 15 days, and behavioral tests were re-evaluated. The brains were obtained and analyzed through immunofluorescence labeling of tyrosine hydroxylase and dopamine D2 receptors. It was observed that rTMS reduces depression-like behaviors. Dopamine D2 receptor density decreased in the dorsal striatum and prefrontal cortex of rats that received treatment compared to those with sham stimulation and untreated animals. These results indicate that rTMS affects not only the stimulated region but also influences the dorsal striatum. This finding might contribute to improving the anti-depressive behavior observed in the chronic unpredictable mild stress rat model.

(E) El Gohary MI, Salama AA, El Saeid AA, El Sayed TM, Kotb HS. Influence of Magnetic Field on Brain Activity During Administration of Caffeine. Cell Biochem Biophys. 67(3):929-933, 2013. (AS, CE, EE)

The aim of the present work is to evaluate the effect of caffeine, the world's most popular psychoactive drug, on the electric activity of the rat's brain that exposed to extremely low-frequency magnetic field (ELF-MF), during 15 days. The obtained results showed that administration of caffeine in a group of rats by dose of 10 mg/kg (equivalent to human daily consumption) caused a reduction in the mean power amplitude of electroencephalogram (EEG) trace for almost all frequency bands especially α (8-12 Hz). It was observed that the influence of caffeine was more evident in motor cortex than in visual cortex. While the exposure of another

group to ELF-MF of intensity 0.2 mT during the same period caused an enhancement in the mean power amplitude of most EEG frequency bands; this was more observed in the right hemisphere of the brain than that of the left hemisphere. The administration of caffeine while rats were exposed to ELF-MF, led, after 5 days of exposure, to a great increase in the mean power amplitude of α band at all places of recording electrodes. It may be concluded that caffeine administration was more effective in reducing the hazardous of ELF-MF in motor cortex than in visual cortex.

(E) Elferchichi M, Ammari M, Maaroufi K, Sakly M, Abdelmelek H. Effects of exposure to static magnetic field on motor skills and iron levels in plasma and brain of rats. Brain Inj. 25(9):901-908, 2011. (AS, CE, CC, BE)

PRIMARY OBJECTIVE: The present work investigated the behavioural and biochemistry effects of moderate exposure to a static magnetic field (SMF) in rats. SMF effects were evaluated in sham- and SMF-exposed rats. **METHODS:** Adult Wistar rats were exposed for 1 hour per day for 5 consecutive days to 128 millitesla (mT) SMF. Then, their motor skills were tested using a Stationary beam and Suspended string test. Iron level in plasma and brain (i.e. frontal cortex, basal ganglia, hippocampus and cerebellum) was measured. **RESULTS:** No significant change was observed between sham and SMF-exposed rats in the Stationary beam and Suspended string test. However, the same treatment induced an increase in plasma transferrin content (+25.4%) and decreased the iron level in plasma (-16.2%). The SMF treatment failed to alter the iron concentration in the brain. **CONCLUSION:** The findings indicate that SMF exposure induced iron deficiency in plasma but did not induce motor-skills deficit.

(E) Erdal ME, Yılmaz SG, Gürgül S, Uzun C, Derici D, Erdal N. miRNA expression profile is altered differentially in the rat brain compared to blood after experimental exposure to 50 Hz and 1 mT electromagnetic field. Prog Biophys Mol Biol. 132:35-42, 2018. (AS, CE, CC)

Common complex diseases are a result of host and environment interactions. One such putative environmental factor is the electromagnetic field exposure, especially the occupational extremely low frequency (ELF) magnetic field, 50 Hz, 1 mT, whose neurobiological relevance remains elusive. We evaluated the effects of long-term (60 days) ELF-MF exposure on miRNAs previously related to brain and human diseases (miR-26b-5p, miR-9-5p, miR-29a-3p, miR-106b-5p, miR-107, miR-125a-3p). A total of 64 young (3 weeks-old) and mature (10 weeks-old) male/female Wistar-Albino rats were divided into sham and ELF-MF exposed groups. After sacrifice of the animals, blood samples from rat's tail vein and brain tissues were collected. The expression levels of miRNAs were investigated with Real-Time PCR technique and TaqMan probe Technology. <u>All miRNA expression levels of the young female rats show a significant decrease in blood according to brain samples ($p < 0.05$), but fewer miRNAs displayed a similar significant decrease in the blood.</u> In conclusion, these new observations might inform future clinical biological psychiatry studies of long-term electromagnetic field exposure, and the ways in which host-environment interactions contribute to brain diseases.

Eskandani R, Zibaii MI. Unveiling the biological effects of radio-frequency and extremely-low frequency electromagnetic fields on the central nervous system performance. Bioimpacts14(4):30064, 2024. (Review)

Introduction: Radiofrequency electromagnetic radiation (RF-EMR) and extremely low-frequency electromagnetic fields (ELF-EMF) have emerged as noteworthy sources of environmental pollution in the contemporary era. The potential biological impacts of RF-EMR and ELF-EMF exposure on human organs, particularly the central nervous system (CNS), have garnered considerable attention in numerous research studies. **Methods:** This article presents a comprehensive yet summarized review of the research on the explicit/implicit effects of RF-EMR and ELF-EMF exposure on CNS performance. **Results:** Exposure to RF-EMR can potentially exert adverse effects on the performance of CNS by inducing changes in the permeability of the blood-brain barrier (BBB), neurotransmitter levels, calcium channel regulation, myelin protein structure, the antioxidant defense system, and metabolic processes. However, it is noteworthy that certain reports have suggested that RF-EMR exposure may confer cognitive benefits for various conditions and disorders. ELF-EMF exposure has been associated with the enhancement of CNS performance, marked by improved memory retention, enhanced learning ability, and potential mitigation of neurodegenerative diseases. Nevertheless, it is essential to acknowledge that ELF-EMF exposure has also been linked to the induction of anxiety states, oxidative stress, and alterations in hormonal regulation. Moreover, ELF-EMR exposure alters hippocampal function, notch signaling pathways, the antioxidant defense system, and synaptic activities. **Conclusion:** The RF-EMR and ELF-EMF exposures exhibit both beneficial and adverse effects. Nevertheless, the precise conditions and circumstances under which detrimental or beneficial effects manifest (either individually or simultaneously) remain uncertain.

(E) Esmaeilpour K, Sheibani V, Shabani M, Mirnajafi-Zadeh J, Akbarnejad Z. Low Frequency Stimulation Reverses the Kindling-Induced Impairment of Learning and Memory in the Rat Passive-avoidance Test. Basic Clin Neurosci. 9(1):51-58, 2018. (AS, CE, BE, MA)

INTRODUCTION: The life quality of patients with epileptic seizures is highly affected by cognitive deficits. Low Frequency Stimulation (LFS) is a novel approach for the treatment of pharmacoresistant epilepsy. The main goal of this research is investigating the possible effect of LFS on seizure-induced cognitive dysfunction. **METHODS:** To this end, the kindled animal were prepared via CA1 electrical stimulation in a semi-rapid way (12 stimulations/day). A group of animals were stimulated with LFS, 4 times at 30 s, 6 h, 24 h, and 30 h after the last kindling stimulation. Applied LFS was administered in 4 packages every 5 minutes. The packages were designed with 200 monophasic 200 monophasic square wave pulses of 0.1 ms duration at 1 Hz. The passive-avoidance test was conducted on all animals in order to measure the learning and memory behavior. **RESULTS:** Hippocampal kindled rats showed deficits in learning and memory when passive avoidance test was performed. Application of LFS reversed the impairment in learning and memory behavior in kindled rats. At the same time, LFS markedly diminished kindling-induced neuronal loss and atrophy in the hippocampus.

CONCLUSION: LFS may have some protection against seizure-induced cognitive damage in kindled rats.

(E) Esmekaya MA, Acar SI, Kıran F, Canseven AG, Osmanagaoglu O, Seyhan N. Effects of ELF magnetic field in combination with Iron(III) chloride (FeCl3) on cellular growth and surface morphology of Escherichia coli (E. coli). Appl Biochem Biotechnol. 169(8):2341-2349, 2013. (CS, AE, MC)

This study investigated the effects of extremely low frequency (ELF) magnetic field with/without iron(III) chloride (FeCl3) on bacterial growth and morphology. The ELF exposures were carried out using a pair of Helmholtz coil-based ELF exposure system which was designed to generate 50 Hz sinusoidal magnetic field. The field was approximately uniform throughout the axis of the coil pair. The samples which were treated or non-treated with different concentrations FeCl3 were exposed to 50 Hz, 2 millitesla (mT) magnetic field for 24 h. ELF effect on viability was assessed in terms of viable colony counts (in colony-forming unit per milliliter) with the standard plate count technique. Scanning electron microscopy was used to investigate the magnetic field effect on surface morphology of Escherichia coli. No significant results were seen in terms of cell viability between ELF and sham-exposed bacterial strains. Similarly, FeCl3 treatment did not change cell viability of E. coli samples. However, we observed some morphological changes on E. coli cell surfaces. Pore formations and membrane destruction were seen on the surface of 24 h ELF field-exposed cells. We concluded that ELF magnetic field exposure at 2 mT does not affect cell viability; however, it may affect bacterial surface morphology.

(E) Falone S, Mirabilio A, Carbone MC, Zimmitti V, Di Loreto S, Mariggiò MA, Mancinelli R, Di Ilio C, Amicarelli F. Chronic exposure to 50Hz magnetic fields causes a significant weakening of antioxidant defence systems in aged rat brain. Int J Biochem Cell Biol. 40(12):2762-2770, 2008. (AS, CE, CC, OX)

Several studies suggest that extremely low-frequency magnetic fields (ELF-MFs) may enhance the free radical endogenous production. It is also well known that one of the unavoidable consequences of ageing is an overall oxidative stress-based decline in several physiological functions and in the general resistance to stressors. On the basis of these assumptions, the aim of this study was to establish whether the ageing process can increase susceptibility towards widely present ELF-MF-mediated pro-oxidative challenges. To this end, female Sprague-Dawley rats were continuously exposed to a sinusoidal 50 Hz, 0.1 mT magnetic field for 10 days. Treatment-induced changes in the major antioxidant protection systems and in the neurotrophic support were investigated, as a function of the age of the subjects. All analyses were performed in brain cortices, due to the high susceptibility of neuronal cells to oxidative injury. Our results indicated that ELF-MF exposure significantly affects anti-oxidative capability, both in young and aged animals, although in opposite ways. Indeed, exposed young individuals enhanced their neurotrophic signalling and anti-oxidative enzymatic defence against a possible ELF-MF-mediated increase in oxygen radical species. In contrast, aged subjects were not capable of increasing their defences in response to ELF-MF treatment but, on the contrary, they

underwent a significant decrease in the major antioxidant enzymatic activities. In conclusion, our data seem to suggest that the exposure to ELF-MFs may act as a risk factor for the occurrence of oxidative stress-based nervous system pathologies associated with ageing.

(E) Falone S, Santini S Jr, Di Loreto S, Cordone V, Grannonico M, Cesare P, Cacchio M, Amicarelli F. Improved Mitochondrial and Methylglyoxal-Related Metabolisms Support Hyperproliferation Induced by 50 Hz Magnetic Field in Neuroblastoma Cells. J Cell Physiol. 231:2014-2025, 2016. (CS, AE, FC)

Extremely low frequency magnetic fields (ELF-MF) are common environmental agents that are suspected to promote later stages of tumorigenesis, especially in brain-derived malignancies. Even though ELF magnetic fields have been previously linked to increased proliferation in neuroblastoma cells, no previous work has studied whether ELF-MF exposure may change key biomolecular features, such as anti-glycative defence and energy re-programming, both of which are currently considered as crucial factors involved in the phenotype and progression of many malignancies. Our study investigated whether the hyperproliferation that is induced in SH-SY5Y human neuroblastoma cells by a 50 Hz, 1 mT ELF magnetic field is supported by an improved defense towards methylglyoxal (MG), which is an endogenous cancer-static and glycating α-oxoaldehyde, and by rewiring of energy metabolism. Our findings show that not only the ELF magnetic field interfered with the biology of neuron-derived malignant cells, by de-differentiating further the cellular phenotype and by increasing the proliferative activity, but also triggered cytoprotective mechanisms through the enhancement of the defense against MG, along with a more efficient management of metabolic energy, presumably to support the rapid cell outgrowth. Intriguingly, we also revealed that the MF-induced bioeffects took place after an initial imbalance of the cellular homeostasis, which most likely created a transient unstable milieu. The biochemical pathways and molecular targets revealed in this research could be exploited for future approaches aimed at limiting or suppressing the deleterious effects of ELF magnetic fields.

Fan Y, Ji X, Zhang L, Zhang X. The Analgesic Effects of Static Magnetic Fields. Bioelectromagnetics 42(2):115-127, 2021. (Review)

Pain is one of the most common reasons why people seek medical care, which is related to most disease states. Magnetic fields (MFs) can be applied locally to specific parts of human bodies with high penetration and temporal control, which have a long-debated history in folk therapy. The purpose of this review is to collect and analyze experimental data about the analgesic effects of static magnetic fields (SMFs) so that we can have a scientific understanding regarding this topic. We collected 28 studies (25 English and 3 Chinese papers) with proper sham controls that investigated the effects of SMFs on pain relief in humans or mice. We found that 64% of the human studies and all mice studies in the literature showed positive analgesic effects of SMFs, which are related to factors including SMF intensity, treatment time, and pain types. Higher intensity and/or longer treatment time, as well as some specific pain types, may have better pain relief effects. Initial mechanistic studies indicated that membrane receptors, such as capsaicin receptor VR1/TRPV1, opioid receptors, and P2X3 receptors, might be involved. By describing experimental evidence and analysis, we found that SMFs actually hold considerable promise for managing some specific types of pain if proper SMF parameters are used. More studies

comprehensively evaluating the parameters of SMF and its corresponding analgesic effects on different pain types, as well as the underlying molecular mechanisms, will be necessary to further validate its therapeutic potential in pain management in the future.

(E) Faraji N, Salehi I, Alizadeh A, Pourgholaminejad A, Komaki A, Taheri Azandaryani M, Sadeghian R, Golipoor Z . Comparing the Effects of Long-term Exposure to Extremely Low-frequency Electromagnetic Fields With Different Values on Learning, Memory, Anxiety, and β-amyloid Deposition in Adult Rats. BCN. 12:849-860, 2021. (AS, CE, CC, OX, BE)

Introduction: Extremely Low-Frequency Electromagnetic Fields (ELF-EMFs) have gathered significant consideration for their possible pathogenicity. However, their effects on the nervous system's functions were not fully clarified. This study aimed to assay the impact of ELF-EMFs with different intensities on memory, anxiety, antioxidant activity, β-amyloid (Aβ) deposition, and microglia population in rats. Methods: Fifty male adult rats were randomly separated into 5 groups; 4 were exposed to a flux density of 1, 100, 500, and 2000 microtesla (μT), 50 Hz frequency for one h/day for two months, and one group as a control group. The control group was without ELF-EMF stimulation. After 8 weeks, passive avoidance and Elevated Plus Maze (EPM) tests were performed to assess memory formation and anxiety-like behavior, respectively. Total free thiol groups and the index of lipid peroxidation were evaluated. Additionally, for detection of Aβ deposition and stained microglia in the brain, anti-β-amyloid and anti-Iba1 antibodies were used. Results: The step-through latency in the retention test in ELF-EMF exposure groups (100, 500 & 2000 μT) was significantly greater than the control group ($P<0.05$). Furthermore, the frequency of the entries into the open arms in ELF-EMF exposure groups (especially 2000 μT) decreased than the control group ($P<0.05$). No Aβ depositions were detected in the hippocampus of different groups. An increase in microglia numbers in the 100, 500, and 2000 μT groups was observed compared to the control and one μT group. Conclusion: Exposure to ELF-EMF had an anxiogenic effect on rats, promoted memory, and induced oxidative stress. No Aβ depositions were detected in the brain. Moreover, the positive impact of ELF-EMF was observed on the microglia population in the brain.

Flatscher J, Lorìè EP, Mittermayr R, Meznik P, Slezak P, Redl H, Slezak C. Pulsed Electromagnetic Fields (PEMF)-Physiological Response and Its Potential in Trauma Treatment. Int J Mol Sci 24(14):11239, 2023. (Review)

Environmental biophysical interactions are recognized to play an essential part in the human biological processes associated with trauma recovery. Many studies over several decades have furthered our understanding of the effects that Pulsed Electromagnetic Fields (PEMF) have on the human body, as well as on cellular and biophysical systems. These investigations have been driven by the observed positive clinical effects of this non-invasive treatment on patients, mainly in orthopedics. Unfortunately, the diversity of the various study setups, with regard to physical parameters, molecular and cellular response, and clinical outcomes, has made it difficult to interpret and evaluate commonalities, which could, in turn, lead to finding an underlying mechanistic understanding of this treatment modality. In this review, we give a birds-eye view of

the vast landscape of studies that have been published on PEMF, presenting the reader with a scaffolded summary of relevant literature starting from categorical literature reviews down to individual studies for future research studies and clinical use. We also highlight discrepancies within the many diverse study setups to find common reporting parameters that can lead to a better universal understanding of PEMF effects.

(E) Fournier NM, Mach QH, Whissell PD, Persinger MA. Neurodevelopmental anomalies of the hippocampus in rats exposed to weak intensity complex magnetic fields throughout gestation. Int J Dev Neurosci. 30:427-433, 2012. (AS, CE, DE, BE, MC)

There has been increasing interest on the possible harmful effects of prenatal exposure to magnetic fields. To investigate the effect of weak intensity magnetic fields on the prenatal brain, pregnant Wistar rats were continuously exposed to one of four intensities (reference: 5-20nT; low 30-50nT; medium 90-580nT; high 590-1200nT) of a complex magnetic field sequence designed to interfere with brain development. As adults, rats exposed to the low-intensity (30-50nT) complex magnetic field displayed impairments in contextual fear learning and showed anomalies in the cytological and morphological development of the hippocampus. In particular, low-intensity exposures resulted in a reduction in overall hippocampal size and promoted subtle dysgenesis of the CA1 and CA3 regions. In contrast, exposure to weaker or stronger intensities of the same complex magnetic field pattern did not interfere with hippocampal development or fear behavior. These findings suggest that prenatal exposure to complex magnetic fields of a narrow intensity window during development can result in subtle but permanent alterations in hippocampal microstructure and function that can have lasting effects on behavior.

(E) Frilot C 2nd, Carrubba S, Marino AA. Transient and steady-state magnetic fields induce increased fluorodeoxyglucose uptake in the rat hindbrain. Synapse. 65(7):617-623, 2011. (HU, AE, CC)

We inquired into the biophysical basis of the ability of weak electromagnetic fields (EMFs) to trigger onset and offset evoked potentials, and to produce steady-state changes in the electroencephalogram (EEG). Rats were exposed to a 2.5-G, 60-Hz magnetic field and the neuroanatomical region of glucose activation associated with the effect of the field on the EEG was identified by positron emission tomography (PET) using fluorodeoxyglucose (FDG). Paired emission scans from the same animal with and without field treatment were differenced and averaged, and t values of the brain voxels computed using the pooled standard deviation were compared with a calculated critical t value to identify the field-activated voxels. Increased glucose utilization occurred in hindbrain voxels when the field was applied orthogonally to the sagittal plane, but not when the angle between the field and the sagittal plane varied randomly. Distinct FDG activation effects were observed in response to transient (both onset and offset) and steady-state magnetic stimuli. Observations of increased glucose utilization induced by magnetic stimuli and its dependence on the direction of the field suggested that signal transduction was mediated by a force detector and that the process and/or early post-transduction processing occurred in the hindbrain.

(E) Frilot C 2nd, Carrubba S, Marino AA. Sensory transduction of weak electromagnetic fields: role of glutamate neurotransmission mediated by NMDA receptors. Neuroscience. 258:184-191, 2014. (AS, AE, EE)

Subliminal electromagnetic fields (EMFs) triggered nonlinear evoked potentials in awake but not anesthetized animals, and increased glucose metabolism in the hindbrain. Field detection occurred somewhere in the head and possibly was an unrecognized function of sensory neurons in facial skin, which synapse in the trigeminal nucleus and project to the thalamus via glutamate-dependent pathways. If so, anesthetic agents that antagonize glutamate neurotransmission would be expected to degrade EMF-evoked potentials (EEPs) to a greater extent than agents having different pharmacological effects. We tested the hypothesis using ketamine which blocks N-methyl-d-aspartate (NMDA) receptors (NMDARs), and xylazine which is an α_2-adrenoreceptor agonist. Electroencephalograms (EEGs) of rats were examined using recurrence analysis to observe EEPs in the presence and absence of ketamine and/or xylazine anesthesia. Auditory evoked potentials (AEPs) served as positive controls. The frequency of observation of evoked potentials in a given condition (wake or anesthesia) was compared with that due to chance using the Fisher's exact test. EEPs were observed in awake rats but not while they were under anesthesia produced using a cocktail of xylazine and ketamine. In another experiment each rat was measured while awake and while under anesthesia produced using either xylazine or ketamine. EEPs and AEPs were detected during wake and under xylazine ($P<0.05$ in each of the four measurements). In contrast, neither EEPs nor AEPs were observed when anesthesia was produced partly or wholly using ketamine. The duration and latency of the EEPs was unaltered by xylazine anesthesia. The afferent signal triggered by the transduction of weak EMFs was likely mediated by NMDAR-mediated glutamate neurotransmission.

(E) Fu Y, Wang C, Wang J, Lei Y, Ma Y. Long-term exposure to extremely low-frequency magnetic fields impairs spatial recognition memory in mice. Clin Exp Pharmacol Physiol. 35(7):797-800, 2008. (AS, CE, BE)

In the present study, we investigated the short- and long-term effects of extremely low-frequency (ELF) magnetic fields on spatial recognition memory in mice by using a two-trial recognition Y-maze that is based on the innate tendency of rodents to explore novel environments. 2. Mice were exposed to 25 or 50 Hz electromagnetic fields for either 7 (short term) or 25 days (long term) and then tested in the Y-maze. 3. The results indicated that neither short- nor long-term exposure to magnetic fields affected the locomotor activity of mice in the Y-maze. However, long-term exposure to 50 Hz fields reduced recognition of the novel arm. 4. Our findings suggest that ELF magnetic fields impair spatial recognition memory in the Y-maze depending on the field strength and/or duration of exposure.

(E) Gallasch E, Rafolt D, Postruznik M, Fresnoza S, Christova M. Decrease of motor cortex excitability following exposure to a 20 Hz magnetic field as generated by a rotating permanent magnet. Clin Neurophysiol. 129(7):1397-1402, 2018. (HU, AE, EE)

OBJECTIVES: Rotation of a static magnet over the motor cortex (MC) generates a transcranial alternating magnetic field (tAMF), and a linked alternating electrical field. The aim of this transcranial magnetic stimulation (TMS) study is to investigate whether such fields are able to influence MC excitability, and whether there are parallels to tACS induced effects.METHODS: Fourteen healthy volunteers received 20 Hz tAMF stimulation over the MC, over the vertex, and 20 Hz tACS over the MC, each with a duration of 15 min. TMS assessments were performed before and after the interventions. Changes in motor evoked potentials (MEP), short interval intra-cortical inhibition (SICI) and intra-cortical facilitation (ICF) were evaluated. RESULTS: The tACS and the tAMF stimulation over the MC affected cortical excitability in a different way. After tAMF stimulation MEP amplitudes and ICF decreased and the effect of SICI increased. After tACS MEP amplitudes increased and there were no effects on SICI and ICF. CONCLUSIONS: The recorded single and paired pulse MEPs indicate a general decrease of MC excitability following 15 min of tAMF stimulation. SIGNIFICANCE: The effects demonstrate that devices based on rotating magnets are potentially suited to become a novel brain stimulation tool in clinical neurophysiology.

(E) Gao Q, Leung A, Yang Y-H, Lau BW, Wang Q, Liao L-Y, Xie Y-J, He C-Q Extremely low frequency electromagnetic fields promote cognitive function and hippocampal neurogenesis of *rats with cerebral ischemia.* Neural Regen Res16(7):1252-1257, 2021.(AS, CE, MC, CC,BE, MA, ND)

Extremely low frequency electromagnetic fields (ELF-EMF) can improve the learning and memory impairment of rats with Alzheimer's disease, however, its effect on cerebral ischemia remains poorly understood. In this study, we established rat models of middle cerebral artery occlusion/reperfusion. One day after modeling, a group of rats were treated with ELF-EMF (50 Hz, 1 mT) for 2 hours daily on 28 successive days. Our results showed that rats treated with ELF-EMF required shorter swimming distances and latencies in the Morris water maze test than those of untreated rats. The number of times the platform was crossed and the time spent in the target quadrant were greater than those of untreated rats. The number of $BrdU^+/NeuN^+$ cells, representing newly born neurons, in the hippocampal subgranular zone increased more in the treated than in untreated rats. Up-regulation in the expressions of Notch1, Hes1, and Hes5 proteins, which are the key factors of the Notch signaling pathway, was greatest in the treated rats. These findings suggest that ELF-EMF can enhance hippocampal neurogenesis of rats with cerebral ischemia, possibly by affecting the Notch signaling pathway.

(E) Gao X, Wang X, Chen F, Qi H, Wang X, Ming D, Zhou P. Research on brain induced effect by extremely low frequency pulsed magnetic stimulation. Conf Proc IEEE Eng Med Biol Soc. 2014:2613-2616, 2014. (HU, AE, EE)

In order to evaluate the influence of extremely low frequency pulsed magnetic fields (ELF PMF) on human brain, we conducted the magnetic stimulation experiments (1 Hz, 10 mT, 20 min), and analyzed the changes of spontaneous EEG activity from 10 subjects. Compared with sham exposure group, the EEG power of theta band (3.5-7.5 Hz) and lower-alpha band (7.5-10 Hz) from the stimulation group increased significantly after magnetic stimulation. By analyzing the latency period and amplitude of P300 in auditory oddball task, we found that the latency period

extended and the amplitude decreased. We suggested that these results might be explained via event-related synchronization induced by magnetic stimulation.

(NE) Gavoçi E, Zironi I, Remondini D, Virelli A, Castellani G, Del Re B, Giorgi G, Aicardi G, Bersani F. ELF magnetic fields tuned to ion parametric resonance conditions do not affect TEA-sensitive voltage-dependent outward K(+) currents in a human neural cell line. Bioelectromagnetics. 34(8):579-88, 2013. (CS, AE, CC)

Despite the experimental evidence of significant biological effects of extremely low frequency (ELF) magnetic fields (MFs), the underlying mechanisms are still unclear. Among the few mechanisms proposed, of particular interest is the so called "ion parametric resonance (IPR)" hypothesis, frequently referred to as theoretical support for medical applications. We studied the effect of different combinations of static (DC) and alternating (AC) ELF MFs tuned on resonance conditions for potassium (K(+)) on TEA-sensitive voltage-dependent outward K(+) currents in the human neuroblastoma BE(2)C cell line. Currents through the cell membrane were measured by whole-cell patch clamp before, during, and after exposure to MF. No significant changes in K(+) current density were found. This study does not confirm the IPR hypothesis at the level of TEA-sensitive voltage-dependent outward K(+) currents in our experimental conditions. However, this is not a direct disprove of the hypothesis, which should be investigated on other ion channels and at single channel levels also.

(E) Geng D, Liu A, Yan Y, Zheng W. Intermittent ELF-MF exposure effectively ameliorates pathologic features associated with adult AD mice. Brain Res. 2025 Jun 20:149796. (AS, CE, CC, EE, BE, MA, ND)

Objective: Extremely low frequency magnetic fields (ELF-MF) have been confirmed to have potentially positive effects on Alzheimer's disease (AD). However, the therapeutic effects are influenced by the exposure mode and the pathological process. Currently, there is no optimized treatment plan for the pathological process of AD. This study aims to optimize the exposure mode of ELF-MF to improve the therapeutic effect on AD mice with different degrees of dementia. **Method:** This study employed 40 Hz, 10mT continuous pulsed ELF-MF stimulation, intermittent (stimulating for 30 min every 12 h) and continuous (stimulating for 60 min every 24 h) ELF-MF exposure. Through calculating various behavioral data, the changes in spatial working memory (SWM) of each group of mice were compared; the time-frequency distribution analysis method was applied to compare the changes in the theta band and gamma band neural oscillations of local field potentials (LFPs) signals in the CA1 region of the hippocampus during the object location task (OLT) of each group of mice; by analyzing the immunofluorescence images of Amyloid-beta 42 ($A\beta_{42}$) and dynamin-related protein 1 (Drp1) in the hippocampal region of each group of mice, the changes in $A\beta_{42}$ and Drp1 contents were compared. **Results:** ELF-MF stimulation can improve the SWM ability of AD model mice. Among them, intermittent stimulation in the adult group shows a better effect, while continuous stimulation in the aged group is superior. Further LFPs analysis reveals that AD leads to a decrease in theta and gamma frequency band energy in the CA1 area of the hippocampus, while ELF-MF stimulation can significantly enhance its energy. Moreover, in the adult group, the improvement of theta and gamma frequency bands under intermittent stimulation is more obvious, and in the aged group,

the improvement of theta frequency band under continuous stimulation is more significant. The results of immunofluorescence detection indicate that ELF-MF stimulation can reduce the abnormal accumulation of $A\beta_{42}$ and Drp1 in the hippocampus, and the effect of intermittent stimulation in the adult group is more significant. **Conclusion:** Intermittent ELF-MF exposure may be an effective therapeutic strategy, especially in adult AD mice. This study highlights the potential significance of the ELF-MF exposure pattern in AD treatment and reveals the heterogeneous effects of ELF-MF exposure on the physiological and pathological conditions of AD mice, which has important guiding significance for the formulation of personalized treatment plans in the future.

(E) Ghassemkhani K, Dotta BT. Can Theta Burst Electromagnetic Fields Disrupt Learning in Planaria? Evidence of Impaired Fear-Conditioned Responses. Bioelectromagnetics. 46(6):e70017, 2025. (AS, AE, BE)

This study explored the impact of low-intensity theta burst patterned electromagnetic fields (TBEMF) on fear-related learning in the flatworm species Planaria, a simple model organism known for its regenerative properties and ability to demonstrate basic learning behaviors. Planaria were exposed to an aversive stimulus (light) in a T-maze, and changes in their behavior, including time taken to select an arm and preferred arm selections, were assessed over the course of several days. The TBEMF consisted of five pulsed bursts at 100 Hz with alternating amplitudes and an intensity of 1 μT. In the group exposed to aversive light, a significant decrease in preferred arm selections was observed ($p < 0.001$), indicating that the planaria successfully learned to avoid the arm associated with the aversive stimulus. However, planaria exposed to TBEMF, either before or after the light exposure phase, did not show the same behavioral adaptation, as their arm selections remained stable, indicating that no fear learning occurred. These findings suggest that TBEMF disrupts the processes involved in fear-related learning, likely by interfering with theta rhythm-dependent mechanisms that are crucial for memory encoding and retrieval. Further exploration of EMF's effects on more complex organisms could reveal additional insights into its broader applications and implications for both basic neuroscience and clinical practice.

(E) Gholami D, Riazi G, Fathi R, Sharafi M, Shahverdi A. Comparison of polymerization and structural behavior of microtubules in rat brain and sperm affected by the extremely low-frequency electromagnetic field. BMC Mol Cell Biol. 20(1):41, 2019. (AS, CE, CC, MC)

BACKGROUND: Microtubule proteins are able to produce electromagnetic fields and have an important role in memory formation, and learning. Therefore, microtubules have the potential to be affected by exogenous electromagnetic fields. This study aimed to examine the comparison of microtubule polymerization and its structural behavior in brain and sperm affected by 50 Hz extremely low-frequency electromagnetic field (ELEF). RESULTS: Twenties adult male rats were randomly and equally divided into control and experimental groups, to evaluate the effect of 50 Hz ELEF on the sperm and brain functions. Plus-maze, serum testosterone and corticosterone, and sperm evaluation were performed. Next, the semen and brain samples were

obtained, and they were divided into four experimental groups for investigation of microtubule polymerization. There was no significant difference in testosterone and, corticosterone levels, anxiety behaviors, and sperm morphology between control and ELEF-exposure groups. The sperm viability, total and progressive motility were significantly higher in the ELEF-exposed group than that of the control group. The microtubule polymerization in sperm ELEF was significantly higher than in other groups. The secondary and tertiary structures of tubulins were significantly affected in the brain, and sperm ELEF groups. CONCLUSION: It seems that the polymerization of microtubules and conformational changes of tubulin dimers are improved by ELEF application

(E) Giorgetto C, Silva EC, Kitabatake TT, Bertolino G, de Araujo JE. Behavioural profile of Wistar rats with unilateral striatal lesion by quinolinic acid (animal model of Huntington disease) post-injection of apomorphine and exposure to static magnetic field. Exp Brain Res. 233(5):1455-1462, 2015. (AS, CE, BE, ND, MA)

We analysed the motor behaviour of Wistar rats after 7 days lesion in the left striatum, injected with apomorphine (APO) and stimulated by a continuous magnetic field of 3,200 Gauss. For the behaviour assessment, we utilised the activity cage test and the rotarod test. Sixty-eight male Wistar rats were divided into six groups: control, sham, sham magnetic, lesion, and stimulated South and North Poles. After the experiments, coronal sections of the striatum were taken and stained with Nissl for analysis of the lesion. In the activity cage test for distance (F = 3.19), time of activity (F = 5.46) and crossings (F = 3.31) in all groups, except for the North Pole-stimulated group, we observed a significant increase in these behaviours when compared to the control group. Considering the number of counterclockwise turns, we observed a significant increase in the lesion in the South and North Pole stimulation groups compared with the control group. Highlighting the minor number of counterclockwise turns observed in the North Pole-stimulated group in relation to the South Pole-stimulated and Lesion groups (F = 16.01). The rotarod test revealed a decrease in the time spent in this apparatus for the Lesion group when compared to all other groups (F = 5.46). The morphometric analysis showed a reduction in the number of neurons in the Lesion group in relation to all other groups (F = 5.13). Thus, the results suggest that the static magnetic field north and south promoted a distinct behavioural profile and morphological preservation after 7 days of lesion with quinolinic acid associated with APO.

(NE) Giorgi G, Lecciso M, Capri M, Lukas Yani S, Virelli A, Bersani F, Del Re B. An evaluation of genotoxicity in human neuronal-type cells subjected to oxidative stress under an extremely low frequency pulsed magnetic field. Mutat Res Genet Toxicol Environ Mutagen. 775-776:31-37, 2014.

The possible genotoxicity of extremely low frequency magnetic field (ELF-MF) exposure is still a controversial topic. The most of the reported data suggests that it alone does not affect DNA integrity, but several recent reports have suggested that sinusoidal ELF-MF may increase the effect of known genotoxic agents. Only a few studies deal with non sinusoidal ELF-MF, including pulsed magnetic field (PMF), which are produced by several devices. The aim of this study is to investigate whether PMF exposure can interfere with DNA damage and repair in the presence of a genotoxic oxidative agent in neuronal type cells. To this purpose gamma-H2AX

foci formation, which is a sensitive marker of DNA double strand breaks (DSB), was investigated at different points of time (1, 24, 48, 72h) after the H2O2 treatment (300µM for 1h) under PMF exposure (1mT, 50Hz) in human neuroblastoma BE(2)C cells. Moreover, cytotoxicity evaluation, by MTT assay and cell cycle analysis, was performed at various points of time after the treatment. Taken together, results suggest that PMF exposure does not interfere with genotoxicity and cytotoxicity induced by oxidative stress.

(NE) Glover PM, Eldeghaidy S, Mistry TR, Gowland PA. Measurement of visual evoked potential during and after periods of pulsed magnetic field exposure. J Magn Reson Imaging. 26(5):1353-1356, 2007. (HU, EE)

PURPOSE: To study the effect of switched magnetic fields used in MR scanners on the visual evoked potential (VEP) in human subjects. MATERIALS AND METHODS: We have used an MRI gradient coil, remote from an MRI magnet to produce a time-varying magnetic field (0.5 kHz, peak field approximately 8.7 T/second) in the human brain without the confounding effects of static field exposure or accompanying acoustic noise. The VEP response to a 2-Hz reversal, 8 x 8 checkerboard, occupying 20 degrees of the visual field was recorded from occipital locations O1 and O2. VEP recordings were made every five minutes before, during, and after a 10-minute magnetic field exposure period for seven subjects. RESULTS: In contradiction to studies previously reported in the literature for fields of 50 Hz and 60 mT, no significant effects on the peak amplitude or latency of the VEP P100 O1 and O2 responses were found. CONCLUSION: Switched magnetic fields of a level and frequency comparable to those used in MRI do not have a significant effect on primary retinal or visual processing.

(E) Goforth KM, Lohmann CMF, Gavin A, Henning R, Harvey A, Hinton TL, Lim DS, Lohmann KJ. Learned magnetic map cues and two mechanisms of magnetoreception in turtles. Nature 2025 Feb 12. doi: 10.1038/s41586-024-08554-y. Online ahead of print. (AS, AE, BE)

Growing evidence indicates that migratory animals exploit the magnetic field of the Earth for navigation, both as a compass to determine direction and as a map to determine geographical position1. It has long been proposed that, to navigate using a magnetic map, animals must learn the magnetic coordinates of the destination2,3, yet the pivotal hypothesis that animals can learn magnetic signatures of geographical areas has, to our knowledge, yet to be tested. Here we report that an iconic navigating species, the loggerhead turtle (Caretta caretta), can learn such information. When fed repeatedly in magnetic fields replicating those that exist in particular oceanic locations, juvenile turtles learned to distinguish magnetic fields in which they encountered food from magnetic fields that exist elsewhere, an ability that might underlie foraging site fidelity. Conditioned responses in this new magnetic map assay were unaffected by radiofrequency oscillating magnetic fields, a treatment expected to disrupt radical-pair-based chemical magnetoreception4-6, suggesting that the magnetic map sense of the turtle does not rely on this mechanism. By contrast, orientation behaviour that required use of the magnetic compass was disrupted by radiofrequency oscillating magnetic fields. The findings provide evidence that two different mechanisms of magnetoreception underlie the magnetic map and magnetic compass in sea turtles.

(E) Gok DK, Akpinar D, Hidisoglu E, Ozen S, Agar A, Yargicoglu P. The developmental effects of extremely low frequency electric fields on visual and somatosensory evoked potentials in adult rats. Electromagn Biol Med. 35(3):245-259, 2016. (AS, CE, EE, OX, EF)

The purpose of our study was to investigate the developmental effects of extremely low frequency electric fields (ELF-EFs) on visual evoked potentials (VEPs) and somatosensory-evoked potentials (SEPs) and to examine the relationship between lipid peroxidation and changes of these potentials. In this context, thiobarbituric acid reactive substances (TBARS) levels were determined as an indicator of lipid peroxidation. Wistar albino female rats were divided into four groups; Control (C), gestational (prenatal) exposure (Pr), gestational+ postnatal exposure (PP) and postnatal exposure (Po) groups. Pregnant rats of Pr and PP groups were exposed to 50 Hz electric field (EF) (12 kV/m; 1 h/day), while those of C and Po groups were placed in an inactive system during pregnancy. Following parturition, rats of PP and Po groups were exposed to ELF-EFs whereas rats of C and Pr groups were kept under the same experimental conditions without being exposed to any EF during 68 days. On postnatal day 90, rats were prepared for VEP and SEP recordings. The latencies of VEP components in all experimental groups were significantly prolonged versus C group. For SEPs, all components of PP group, P2, N2 components of Pr group and P1, P2, N2 components of Po group were delayed versus C group. As brain TBARS levels were significantly increased in Pr and Po groups, retina TBARS levels were significantly elevated in all experimental groups versus C group. In conclusion, alterations seen in evoked potentials, at least partly, could be explained by lipid peroxidation in the retina and brain.

(E) Goraghani MS, Ahmadi-Zeidabadi M, Bakhshaei S, Shabani M, Ravandi SG, Zarchi SR, Nozari M. Behavioral consequences of simultaneous postnatal exposure to MK-801 and static magnetic field in male Wistar rats. Neurosci Lett 701:77-83, 2019.(AS, CE, BE, IX)

Various experimental studies reported some neurobehavioral adverse effects of static magnetic field (SMF) exposure. The reason is unclear, but one of the possibilities might be alternations in the level of the neurotransmitters and their receptors. Considering the critical role of N-Methyl D-aspartate (NMDA) receptors in the molecular regulation of cognition, motor control, and synaptic plasticity, it is important to investigate interactions between SMF exposure and administration of NMDA receptor blockers such as MK-801. Now, we administered low-dose (0.1 mg/kg) MK-801 to the male Wistar rats, from postnatal day (P) 6 to 10 and investigate whether its effects change under the influence of SMF exposure. Morris water maze, open field test, rotarod, and elevated plus maze tests were performed on P60-63 to evaluate long-term effects on learning and memory, locomotion activities, and anxiety-like behaviors. Our results showed that administration of low-dose MK-801 did not lead to significant adverse effects on their long-term anxiety-like behaviors, locomotion, learning, and memory; however, simultaneous exposure to SMF can result in these adverse effects. In conclusion, exposure to SMF can augment the neurobehavioral effects of MK-801, by enhancing the blockage of the NMDA receptors. Further studies are required to confirm these results.

(E) Grob R, Müller VL, Grübel K, Rössler W, Fleischmann PN. Importance of magnetic information for neuronal plasticity in desert ants. Proc Natl Acad Sci U S A 121(8):e2320764121, 2024. (AS, AE, FC, BC, EE) (0.5 mG and 1 mG)

Many animal species rely on the Earth's magnetic field during navigation, but where in the brain magnetic information is processed is still unknown. To unravel this, we manipulated the natural magnetic field at the nest entrance of *Cataglyphis* desert ants and investigated how this affects relevant brain regions during early compass calibration. We found that manipulating the Earth's magnetic field has profound effects on neuronal plasticity in two sensory integration centers. Magnetic field manipulations interfere with a typical look-back behavior during learning walks of naive ants. Most importantly, structural analyses in the ants' neuronal compass (central complex) and memory centers (mushroom bodies) demonstrate that magnetic information affects neuronal plasticity during early visual learning. This suggests that magnetic information does not only serve as a compass cue for navigation but also as a global reference system crucial for spatial memory formation. We propose a neural circuit for integration of magnetic information into visual guidance networks in the ant brain. Taken together, our results provide an insight into the neural substrate for magnetic navigation in insects.

Guerriero F, Ricevuti G. Extremely low frequency electromagnetic fields stimulation modulates autoimmunity and immune responses: a possible immuno-modulatory therapeutic effect in neurodegenerative diseases. Neural Regen Res. 11(12):1888-1895, 2016. (Review)

Increasing evidence shows that extremely low frequency electromagnetic fields (ELF-EMFs) stimulation is able to exert a certain action on autoimmunity and immune cells. In the past, the efficacy of pulsed ELF-EMFs in alleviating the symptoms and the progression of multiple sclerosis has been supported through their action on neurotransmission and on the autoimmune mechanisms responsible for demyelination. Regarding the immune system, ELF-EMF exposure contributes to a general activation of macrophages, resulting in changes of autoimmunity and several immunological reactions, such as increased reactive oxygen species-formation, enhanced phagocytic activity and increased production of chemokines. Transcranial electromagnetic brain stimulation is a non-invasive novel technique used recently to treat different neurodegenerative disorders, in particular Alzheimer's disease. Despite its proven value, the mechanisms through which EMF brain-stimulation exerts its beneficial action on neuronal function remains unclear. Recent studies have shown that its beneficial effects may be due to a neuroprotective effect on oxidative cell damage. On the basis of *in vitro* and clinical studies on brain activity, modulation by ELF-EMFs could possibly counteract the aberrant pro-inflammatory responses present in neurodegenerative disorders reducing their severity and their onset. The objective of this review is to provide a systematic overview of the published literature on EMFs and outline the most promising effects of ELF-EMFs in developing treatments of neurodegenerative disorders. In this regard, we review data supporting the role of ELF-EMF in generating immune-modulatory responses, neuromodulation, and potential neuroprotective benefits. Nonetheless, we reckon that the underlying mechanisms of interaction between EMF and the immune system are still to be completely understood and need further studies at a molecular level.

(E) Guleken Z, Kula-Maximenko M, Depciuch J, Kılıç AM, Sarıbal D. Detection of the chemical changes in blood, liver, and brain caused by electromagnetic field exposure using Raman spectroscopy, biochemical assays combined with multivariate analyses. Photodiagnosis Photodyn Ther 38:102779, 2022. (AS, CE, MC, CC, OX, DE)

The effects of the electromagnetic field on living organisms have been studied for several years. In this article, we showed what kind of cold change an extremely low-frequency electromagnetic field (ELF-MF) exposure 500 µT 50 Hz by using a Meritt Coil System causes in the samples of the brain and liver samples. To measure oxidative load, we measured malondialdehyde (MDA) and glutathione (GSH) levels. To identify the chemical changes, we collected Raman spectra of cerebellum, left brain, right brain and liver tissue from the control group of animals and from the animal, which were exposed to an electromagnetic field (ELF-MF group). Obtained results showed, that lipid peroxidation was increased and the antioxidant response was decreased. In the brain samples the shift of peaks corresponding to the amide III vibrations existed after ELF-MF exposure. Structural changes were detected in CH_2 vibrations originating from lipids in both hemispheres. Additionally, the number of amide III bonds was increased with ELF-MF exposure in the cerebellum and left-brain tissue. In liver tissue higher Raman intensities were visible in the tissues from the ELF-MF group. In this group electromagnetic field also caused structural changes in lipids. Principal component analysis (PCA) showed, that it is possible to distinguish ELF-MF and control groups. Consequently, hierarchical component analysis (HCA) showed that tissues from ELF-MF and control groups separately created similarity with the groups. Obtained results suggest that the electromagnetic field caused structural and quantitative chemical changes in brain and liver tissue. Additionally, present data suggest that ELF-MF plays an important role in the regulation of enzyme activity and has effects on biochemical processes, possibly improved by production of ROS.

(E) Gülmez K, Demirkazık A, Taşkıran AŞ. Effect of ELF-EMF on cognitive functions, analgesia, and oxidative stress in rats with PTZ-induced epilepsy. Electromagn Biol Med. 2025 Nov 27:1-11. doi: 10.1080/15368378.2025.2593267. Epub ahead of print. (AS, CE, BE, OX, IX)

This study aimed to examine the impacts of extremely low-frequency (ELF)-electromagnetic field (EMF) on cognitive functions and analgesia in terms of total oxidant status (TOS) and total antioxidant status (TAS) in the experimental pentylenetetrazole (PTZ)-induced epilepsy model. Twenty-four Wistar albino male rats were categorized into four groups: sham, EMF, PTZ, and EMF+PTZ. The rats were repeatedly exposed to alternating 50-Hz and 5-mT EMF for 165 min a day for 7 days. Epileptic seizures were induced with PTZ. The levels of oxidative stress markers were measured. Univariate multifactorial one-way analysis of variance and post hoc Tukey's test were used for pairwise comparisons between groups. A statistically significant difference was observed in the learning and short-term memory levels in the EMF + PTZ group compared with the PTZ group ($p < 0.001$). Analgesia latency statistically significantly increased in the ELF-EMF and ELF-EMF+PTZ groups compared with both the control and epilepsy groups ($p < 0.001$). A statistically significant increase in TOS was found in the prefrontal cortex in the PTZ group compared with the sham group ($p < 0.001$). Also, TOS statistically significantly increased in the hippocampus in both PTZ and ELF-EMF+ PTZ groups compared with the sham group ($p < 0.001$). ELF-EMF decreased the increased TOS in the hippocampus of rats in the PTZ group.

(E) Gulturk S, Demirkazik A, Kosar I, Cetin A, Dökmetas HS, Demir T. Effect of exposure to 50 Hz magnetic field with or without insulin on blood-brain barrier permeability in streptozotocin-induced diabetic rats. Bioelectromagnetics. 31(4):262-269, 2010. (AS, CE, ME)

We investigated the effect of long-term exposure to modulation magnetic field (MF), insulin, and their combination on blood-brain barrier (BBB) permeability in a diabetic rat model. Fifty-three rats were randomly assigned to one of six groups: sham, exposed to no MF; MF, exposed to MF; diabetes mellitus (DM), DM induced with streptozotocin (STZ); DM plus MF (DMMF); DM plus insulin therapy (DMI); and DM plus insulin therapy plus MF (DMIMF). All the rats underwent Evans blue (EB) measurement to evaluate the BBB 30 days after the beginning of experiments. The rats in MF, DMMF, and DMIMF groups were exposed to MF (B = 5 mT) for 165 min every day for 30 days. Mean arterial blood pressure (MABP), body mass, and serum glucose level of the study rats were recorded. The extravasation of brain EB of the MF, DM, DMMF, DMI, and DMIMF groups was higher than that of the sham group and the extravasation of right hemisphere of the DMIMF group was highest ($P < 0.05$). The post-procedure body mass of the sham and MF groups were significantly higher than those of the DM and DMMF groups ($P < 0.05$). In the DM, DMMF, DMI, and DMIMF groups, the baseline glucose was significantly lower than the post-procedure glucose ($P < 0.05$). DM and MF increase BBB permeability; in combination, they cause more increase in BBB permeability, and insulin decreases their effect on BBB. Improved glucose metabolism may prevent body mass loss and the hypoglycemic effect of MF. DM increases MABP but MF causes no additional effect.

(E) Gao M, Peng H, Hou Y, Wang X, Li J, Qi H, Kuang F, Zhang J. Electromagnetic pulse induced blood-brain barrier breakdown through tight junction opening in rats. Bioelectromagnetics 45:130-138, 2024. (AS, AE, MC, CC, FC)

The blood-brain barrier (BBB) is the main obstacle to hydrophilic and large molecules to enter the brain, maintaining the stability of the central nervous system (CNS). But many environmental factors may affect the permeability and structure of the BBB. Electromagnetic pulses (EMP) irradiation has been proven to enhance the permeability of the BBB, but the specific mechanism is still unclear. To explore the potential mechanism of EMP-induced BBB opening, this study investigated the permeability, fine structure and the proteins expression of the tight junction (TJ) of the BBB in the rats exposed to EMP. Using the leakage of fluorescein isothiocyanate-labeled dextran with different molecular mass under different field intensity of EMP exposure, we found that the tracer passing through the BBB is size-dependent in the rat exposed to EMP as field intensity increased. Transmission electron microscopy showed TJ of the endothelial cells in the EMP-exposed group was open, compared with the sham-irradiated group. But the levels of TJ proteins including ZO-1, claudin-5, or occludin were not changed as indicated by western blot. These data suggest that EMP induce BBB opening in a field intensity-dependent manner and probably through dysfunction of TJ proteins instead of their expression. Our findings increase the understanding of the mechanism for EMP working on the brain and are helpful for CNS protection against EMP.

(E) Guo, Y., FU, Y, Sun W. 50 Hz Magnetic Field Exposure Inhibited Spontaneous Movement of Zebrafish Larvae through ROS-Mediated syn2a Expression. Int. J. Mol. Sci. 24(8), 7576, 2023. (AS, CE, BE, OX)

Extremely low frequency electromagnetic field (ELF-EMF) exists widely in public and occupational environments. However, its potential adverse effects and the underlying mechanism on nervous system, especially behavior are still poorly understood. In this study, zebrafish embryos (including a transfected synapsin IIa (syn2a) overexpression plasmid) at 3 h post-fertilization (hpf) were exposed to a 50-Hz magnetic field (MF) with a series of intensities (100, 200, 400 and 800 μT, respectively) for 1 h or 24 h every day for 5 days. Results showed that, although MF exposure did not affect the basic development parameters including hatching rate, mortality and malformation rate, yet MF at 200 μT could significantly induce spontaneous movement (SM) hypoactivity in zebrafish larvae. Histological examination presented morphological abnormalities of the brain such as condensed cell nucleus and cytoplasm, increased intercellular space. Moreover, exposure to MF at 200 μT inhibited syn2a transcription and expression, and increased reactive oxygen species (ROS) level as well. Overexpression of syn2a could effectively rescue MF-induced SM hypoactivity in zebrafish. Pretreatment with N-acetyl-L-cysteine (NAC) could not only recover syn2a protein expression which was weakened by MF exposure, but also abolish MF-induced SM hypoactivity. However, syn2a overexpression did not affect MF-increased ROS. Taken together, the findings suggested that exposure to a 50-Hz MF inhibited spontaneous movement of zebrafish larvae via ROS-mediated syn2a expression in a nonlinear manner.

(E) Gutiérrez-Mercado YK, Cañedo-Dorantes L, Gómez-Pinedo U, Serrano-Luna G, Bañuelos-Pineda J, Feria-Velasco A. Increased vascular permeability in the circumventricular organs of adult rat brain due to stimulation by extremely low frequency magnetic fields. Bioelectromagnetics. 34(2):145-155, 2013. (AS, CE, MC)

It has been demonstrated that the exposure of biological systems to magnetic fields (MFs) can produce several beneficial effects: tissue recovery in chronic wounds, re-establishment of blood circulation after tissue ischemia or in necrotic tissues, improvement after epileptic episodes, angiogenesis, etc. In the current study, the effects of extremely low frequency (ELF) MF on the capillaries of some circumventricular organs (CVOs) are demonstrated; a vasodilator effect is reported as well as an increase in their permeability to non-liposoluble substances. For this study, 96 Wistar male rats (250 g body mass) were used and divided into three groups of 32 rats each: a control group (no treatment); a sham ELF-MF group; and an experimental group subjected to ELF-MF (120 Hz harmonic waves and 0.66 mT, root mean square) by the use of Helmholtz coils. All animals were administered colloidal carbon (CC) intravenously to study, through optical and transmission electron microscopy, the capillary permeability in CVOs and the blood-brain barrier (BBB) in brain areas. An increase in capillary permeability to CC was detected in the ELF-MF-exposed group as well as a significant increase in vascular area (capillary vasodilation); none of these effects were observed in individuals of the control and sham ELF-MF groups. It is important to investigate the mechanisms involved in the phenomena reported here in order to explain the effects of ELF-MF on brain vasculature.

(NE) Hadzibegovic S, Nicole O, Andelkovic V, de Gannes FP, Hurtier A, Lagroye I, Bontempi B. Examining the effects of extremely low-

frequency magnetic fields on cognitive functions and functional brain markers in aged mice. Sci Rep15(1):8365, 2025. (AS, CE, CC, BE)

Extremely low-frequency magnetic fields (ELF-MFs) are ubiquitously present in various environments of everyday life. While surveys from the World Health Organization (WHO) have not demonstrated the existence of ELF-MF-induced harmful consequences in healthy subjects, whether older adults are more vulnerable to the effects of residential and occupational ELF-MF exposure, and therefore may be at risk, remains unsettled. Here, we explored this potential health issue by investigating, in aged mice, the effects of chronic exposure to ELF-MFs (50 Hz ELF-MF at 1 mT for 8 h/day, 5 days/week for 12 consecutive weeks) on cognitive functions and expression profile of brain markers typically associated with aggravated aging or the development of Alzheimer`s disease (AD). Sham-exposed mice showed a significant age-related decline in spatial memory functions compared to young adult mice. However, this expected pattern was neither exacerbated nor counteracted by chronic exposure to ELF-MFs. No difference in hippocampal expression of APP-695, Aβ(1-42), S100b and GFAP proteins or in the pTau/Tau ratio was observed between sham- and ELF-MF-exposed aged mice, suggesting that chronic exposure to ELF-MFs does not aggravate aging and associated neuroinflammation, or promote pathological pathways involved in the initiation of AD. Because care should be taken in extrapolating these results to older adults with various comorbidities, applying current exposure limits to existing or new sensitive ELF-MF locations is recommended.

(E) Haghighat N, Abdolmaleki P, Parnian J, Behmanesh M. The expression of pluripotency and neuronal differentiation markers under the influence of electromagnetic field and nitric oxide. Mol Cell Neurosci. 85:19-28, 2017. (CS, AE, MC)

Nitric oxide (NO) is a diatomic free radical compound that as a secondary messenger contributes to cell physiological functions and its variations influence proteins activity and triggering intracellular signaling cascades. Low frequency electromagnetic field (EMF) alters the cell biology such as cell differentiation by targeting the plasma membrane and entering force to the ions and small electrical ligands. The effect of these chemical (NO) and physical (EMF) factors on the expression of the stemness and neuronal differentiation markers in rat bone marrow mesenchymal stem cells (BMSC) was investigated. The cells were treated with low (50micromolar) and high (1mM) concentrations of Deta-NO as a NO donor molecule and 50Hz low frequency EMF. The expression of pluripotency and neuronal differentiation genes and proteins was investigated using real time qPCR and Immunocytochemistry techniques. The simultaneous treatment of EMF with NO (1mM) led to the down-regulation of stemness markers expression and up-regulation of neuronal differentiation markers expression. Cell proliferation decreased and cell morphology changed which caused the majority of cells obtains neuronal protein markers in their cytoplasm. The decrease in the expression of neuronal differentiation Nestin and DCX markers without any change in the expression of pluripotency Oct4 marker (treated with low concentration of NO) indicates protection of stemness state in these cells. Treatment with NO demonstrated a double behavior. NO low concentration helped the cells protect the stemness state but NO high concentration plus EMF pushed cells into differentiation pathway.

Hales CG. The origins of the brain's endogenous electromagnetic field and its relationship to provision of consciousness. J Integr Neurosci. 13(2):313-361, 2014. (opinion)

As a potential source of consciousness, the brain's endogenous electromagnetic (EM) field has much to commend it. Difficulties connecting EM phenomena and consciousness have been exacerbated by the lack of a specific conclusive biophysically realistic mechanism originating the EM field, its form and dynamics. This work explores a potential mechanism: the spatial and temporal coherent action of transmembrane ion channel currents which simultaneously produce electric and magnetic fields that dominate all other field sources. Ion channels, as tiny current filaments, express, at a distance, the electric and magnetic fields akin to those of a short (transmembrane) copper wire. Following assembly of appropriate formalisms from EM field theory, the paper computationally explores the scalar electric potential produced by the current filaments responsible for an action potential (AP) in a realistic hippocampus CA1 pyramidal neuron. It reveals that AP signaling can impress a highly structured, focused and directed "sweeping-lighthouse beam" that "illuminates" neighbors at mm scales. Ion channel currents thereby provide a possible explanation for both EEG/MEG origins and recently confirmed functional EM coupling effects. Finally, a physically plausible EM field decomposition is posited. It reveals objective and subjective perspectives intrinsic to the membrane-centric field dynamics. Perceptual "fields" can be seen to operate as the collective action of virtual EM-boson composites (called qualeons) visible only by "being" the fields, yet objectively appear as the familiar EM field activity. This explains the problematic evidence presentation and offers a physically plausible route to a solution to the "hard problem".

(E) Harakawa S, Nedachi T, Hori T, Takahashi K, Tochio K, Inoue N. Effect of electric field in conditioned aversion response. J Vet Med Sci. 70(6):611-613, 2008. (AS, AE, BE, EF)

The aim of the present study was to estimate whether rat sense exogenous electric field (EF) including one used in our previous studies. Employing a conditioned place aversion response paradigm based on an aversive behavior against light environment, alteration in both voluntary behavior of Wistar rat to a 50 Hz sinusoidal EF was examined. Following conditioning without EF, the times spent in white place in rats was significantly shortened ($P<0.05$). While, such changes were not shown in rats conditioned with EF. Thus, it was considered that the aversion response to light environment was interfered by exposure to EF. An interference in recognition of brightness via EF induced effect to visual system or in learning system via direct effect to central nerve system was considerable as a factor for EF-induced effect. In addition, it was remained that rat possibly sense exposure to EF as preferable. In order to confirm which factor functioned, further studies are needed.

(E) Harakawa S, Nedachi T, Shinba T, Suzuki H.Stress-Reducing Effect of a 50 Hz Electric Field in Mice after Repeated Immobilizations, Electric Field Shields, and Polarization of the Electrodes. Biology (Basel) 11(2):323, 2022.(AS, AE, CC, IX)

In BALB/c mice, immobilization-increased plasma glucocorticoid (GC) levels are suppressed by extremely low frequency (ELF) electric fields (EF). The aim of this study was to advance our understanding of the biological effects of ELF-EF, using its suppressive effect on the GC response. Mice were exposed to a 50 Hz EF of 10 kV/m via a parallel plate electrode and

immobilized as needed. We examined the suppressive effect of ELF-EF on GC level change after repeated immobilizations, electrode polarization, and EF shielding of different portions of the mouse body parts. Additionally, bodyweight changes owing to stress and EF were examined. Immobilization-induced reduction in the plasma GC levels was reproduced in mice with stress and EF exposure, regardless of the stress episode numbers and electrode polarization. Furthermore, when the head of mice was shielded from the EF, the suppressive effect was possibly relatively lower than that when the abdomen was shielded. The bodyweight of the mice decreased for 3 days after immobilization before recovering; ELF-EF did not affect the bodyweight. Thus, to elicit the biological effects of the EF, not only the size of the area where the EF is distributed but also the area where the field is distributed should be important. The results also confirmed the stableness of the present experimental system, at least in terms of the stress-reducing effect. In addition, the restriction in this study caused weight loss, but ELF-EF was not considered to affect it. The results improve the understanding of the biological effect and medical applications of ELF-EF

(E) He LH, Shi HM, Liu TT, Xu YC, Ye KP, Wang S. Effects of extremely low frequency magnetic field on anxiety level and spatial memory of adult rats. Chin Med J (Engl). 124(20):3362-3366, 2011. (AS, CE, BE)

BACKGROUND: As the widespread use of electric devices in modern life, human are exposed to extremely low frequency magnetic fields (ELF MF) much more frequently than ever. Over the past decades, a substantial number of epidemiological and experimental studies have demonstrated that ELF MF (50 Hz) exposure is associated with increased risk of various health effects. The present study examined the effects of chronic exposure to ELF MF on anxiety level and spatial memory of adult rats. METHODS: The 50-Hz ELF MF was used during the whole experimental procedures and the value of magnetic field (MF) was set to 2 mT. Adult rats were divided randomly to control, MF 1 hour and MF 4 hours group. Anxiety-related behaviors were examined in the open field test and the elevated plus maze; changes in spatial learning and memory were determined in Morris water maze after 4 weeks of daily exposure. RESULTS: Rats in MF 4 hours group had increased anxiety-like behaviors with unaltered locomotor activity. In the Morris water maze test, rats had reduced latency to find the hidden platform and improved long-term memory of former location of platform without changes in short-term memory and locomotor activity. CONCLUSION: Chronic ELF MF exposure has anxiogenic effect on rats, and the promoting effects on spatial learning and long-term retention of spatial memory.

(E) He Y, Sun W, Leung PS, Chow YT. Effect of Static Magnetic Field of Electric Vehicles on Driving Performance and on Neuro-Psychological Cognitive Functions. Int J Environ Res Public Health. 16(18):3382, 2019. (HU, AE, BE)

Human neuropsychological reactions and brain activities when driving electric vehicles (EVs) are considered as an issue for traffic and public safety purposes; this paper examined the effect of the static magnetic field (SMF) derived from EVs. A lane change task was adopted to evaluate the driving performance; and the driving reaction time test and the reaction time test were adopted to evaluate the variation of the neuro-psychological cognitive functions. Both the sham

and the real exposure conditions were performed with a 350 μT localized SMF in this study; 17 student subjects were enrolled in this single-blind experiment. Electroencephalographs (EEGs) of the subjects were adopted and recorded during the experiment as an indicator of the brain activity for the variations of the driving performance and of the cognitive functions. Results of this study have indicated that the impact of the given SMF on both the human driving performance and the cognitive functions are not considerable; and that there is a correlation between beta sub-band of the EEGs and the human reaction time in the analysis.

(NE) He YL, Liu DD, Fang YJ, Zhan XQ, Yao JJ, Mei YA. Exposure to extremely low-frequency electromagnetic fields modulates Na+ currents in rat cerebellar granule cells through increase of AA/PGE2 and EP receptor-mediated cAMP/PKA pathway. PLoS One. 8(1):e54376, 2013. (CS, AE, CC, EE)

Although the modulation of Ca(2+) channel activity by extremely low-frequency electromagnetic fields (ELF-EMF) has been studied previously, few reports have addressed the effects of such fields on the activity of voltage-activated Na(+) channels (Na(v)). Here, we investigated the effects of ELF-EMF on Na(v) activity in rat cerebellar granule cells (GCs). Our results reveal that exposing cerebellar GCs to ELF-EMF for 10-60 min significantly increased Na(v) currents (I(Na)) by 30-125% in a time- and intensity-dependent manner. The Na(v) channel steady-state activation curve, but not the steady-state inactivation curve, was significantly shifted (by 5.2 mV) towards hyperpolarization by ELF-EMF stimulation. This phenomenon is similar to the effect of intracellular application of arachidonic acid (AA) and prostaglandin E(2) (PGE(2)) on I(Na) in cerebellar GCs. Increases in intracellular AA, PGE(2) and phosphorylated PKA levels in cerebellar GCs were observed following ELF-EMF exposure. Western blottings indicated that the Na(V) 1.2 protein on the cerebellar GCs membrane was increased, the total expression levels of Na(V) 1.2 protein were not affected after exposure to ELF-EMF. Cyclooxygenase inhibitors and PGE(2) receptor (EP) antagonists were able to eliminate this ELF-EMF-induced increase in phosphorylated PKA and I(Na). In addition, ELF-EMF exposure significantly enhanced the activity of PLA(2) in cerebellar GCs but did not affect COX-1 or COX-2 activity. Together, these data demonstrate for the first time that neuronal I(Na) is significantly increased by ELF-EMF exposure via a cPLA2 AA PGE(2) EP receptors PKA signaling pathway.

(E) Hermans A, Maris T, Hubert J, Rochas C, Scott K, Murk AJ, Winter HV. From subsea power cable to small-spotted catshark Scyliorhinus canicula: Behavioural effects of electromagnetic fields in tank experiments. Mar Environ Res. 208:107127, 2025. (AS, CE, BE)

Subsea power cables are expanding in number and capacity due to increasing demand to transport offshore generated energy. Energy transported through a cable creates an electromagnetic field (EMF). Elasmobranchs are dependent on their perception of the earth's magnetic field and biologically induced electric fields, for orientation, navigation, locating conspecifics and detecting prey. EMF levels from subsea power cables will add to natural signals potentially disrupting elasmobranch perception, but the effects are not fully understood. Reported behavioural responses include attraction, disturbance, and indifference, varying with

exposure type, level and experimental set-up. In this study, the effects of EMF on swimming behaviour of 14 individual small-spotted catshark Scyliorhinus canicula were studied. All sharks were exposed to field-relevant EMF gradients cables in three trials: 15.0 µT AC, 19.6 µT DC, and a control treatment. Sharks showed no startle response to EMF onset, did not alter movement towards or away from the cable, and crossed it as frequently as in control trials. Hidden Markov Models showed that behavioural states were best explained by EMF treatment, trial order and sex. Sharks showed 25 % less time transiting during DC trials when compared to AC and control trials. These findings indicate reason for further refined studies to better determine behavioural effects from direct current subsea power cables with S. canicula, for example using tagging studies. In addition, exploring effects on other species will help obtain a broader understanding of the potential impacts of EMF on benthic elasmobranchs.

(E) Hernádi L, László JF. Pharmacological analysis of response latency in the hot plate test following whole-body static magnetic field-exposure in the snail Helix pomatia. Int J Radiat Biol. 90(7):547-553, 2014. (AS, AE, CE, BE)

Purpose: The effect of single, 30 min long, whole-body static magnetic field (SMF)-exposure on the response latency of the snail Helix pomatia has been the focus of this study. Materials and methods: The response was investigated using the hot plate test. Results: The effect caused by exposure to homogeneous SMF (147±3 mT) was compared to sham-exposure and resulted in significant differences (up to 47.1%, $p<0.001$). The response latency depended on the day-night cycle; response latency was higher by 51.2% ($p<0.001$) during the night. This trend also held for SMF-exposure (28.6%, $p<0.001$). Serotonin alone increased response latency (55.7%, $p<0.001$), whereas serotonin antagonist tryptamine decreased it (-97.8%, $p<0.001$). Using naloxone, response latency decreased (-52.5%, $p<0.001$); however both SMF-exposure and serotonin in combination with naloxone rose it back to above the control level (116. 9%, $p<0.001$ or 150.2%, $p<0.001$, respectively). Conclusions: This study provides evidence that SMF-exposure mediates peripheral thermal nociceptive threshold by affecting the serotonerg as well as the opioiderg system.

(E) Hong I, Garrett A, Maker G, Mullaney I, Rodger J, Etherington SJrkip. Repetitive low intensity magnetic field stimulation in a neuronal cell line: a metabolomics study. PeerJ. 6:e4501, 2018. (CS, AE, CC)

Low intensity repetitive magnetic stimulation of neural tissue modulates neuronal excitability and has promising therapeutic potential in the treatment of neurological disorders. However, the underpinning cellular and biochemical mechanisms remain poorly understood. This study investigates the behavioural effects of low intensity repetitive magnetic stimulation (LI-rMS) at a cellular and biochemical level. We delivered LI-rMS (10 mT) at 1 Hz and 10 Hz to B50 rat neuroblastoma cells *in vitro* for 10 minutes and measured levels of selected metabolites immediately after stimulation. LI-rMS at both frequencies depleted selected tricarboxylic acid (TCA) cycle metabolites without affecting the main energy supplies. Furthermore, LI-rMS effects were frequency-specific with 1 Hz stimulation having stronger effects than 10 Hz. The observed depletion of metabolites suggested that higher spontaneous activity may have led to an

increase in GABA release. Although the absence of organised neural circuits and other cellular contributors (e.g., excitatory neurons and glia) in the B50 cell line limits the degree to which our results can be extrapolated to the human brain, the changes we describe provide novel insights into how LI-rMS modulates neural tissue.

Hosseini E. Ubiquitous extremely low frequency electromagnetic fields induces anxiety-like behavior: mechanistic perspectives. Electromagn Biol Med 2024 Jul 29:1-16. doi: 10.1080/15368378.2024.2380305. Online ahead of print. (Review)

Anxiety is an adaptive condition characterized by heightened uneasiness, which in the long term can cause complications such as reducing the quality of life and problems related to the mental and physical health. Concerns have been raised regarding the potential dangers of extremely low frequency electromagnetic fields (ELF-EMF) ranging from 3 to 3000 Hz, which are omnipresent in our daily lives and there have been studies about the anxiogenic effects of these fields. Studies conducted in this specific area has revealed that ELF-EMF can have an impact on various brain regions, such as the hippocampus. In conclusion, studies have shown that ELF-EMF can interfere with hippocampus-prefrontal cortex pathway, inducing anxiety behavior. Also, ELF-EMF may initiate anxiety behavior by generating oxidative stress in hypothalamus and hippocampus. Moreover, ELF-EMF may induce anxiety behavior by reducing hippocampus neuroplasticity and increasing the NMDA2A receptor expression in the hippocampus. Furthermore, supplementation with antioxidants could serve as an effective protective measure against the adverse effects of FLF-FMF in relation to anxiety behavior.

(E)Hosseini E, M.F. Habibi, S. Babri, G. Mohaddes, H. Abkhezr, H. Heydari. Maternal stress induced anxiety-like behavior exacerbated by electromagnetic fields radiation in female rats offspring. PLoS One 17(8):e0273206, 2022. (AS, CE, CC, BE, IX)

There is a disagreement on whether extremely low frequency electromagnetic fields (ELF-EMF) have a beneficial or harmful effect on anxiety-like behavior. Prenatal stress induces frequent disturbances in offspring physiology such as anxiety-like behavior extending to adulthood. This study was designed to evaluate the effects of prenatal stress and ELF-EMF exposure before and during pregnancy on anxiety-like behavior and some anxiety-related pathways in the hippocampus of female rat offspring. A total of 24 female rats 40 days of age were distributed into four groups of 6 rats each: control, Stress (rats whose mothers underwent chronic stress), EMF (rats whose mothers were exposed to electromagnetic fields) and EMF/S (rats whose mothers were simultaneously exposed to chronic stress and ELF-EMF). The rats were given elevated plus-maze and open field tests and then their brains were dissected and their hippocampus were subjected to analysis. ELISA was used to measure 24(S)-hydroxy cholesterol, corticosterone, and serotonin levels. Cryptochrome2, steroidogenic acute regulatory protein, 3B-Hydroxy steroid dehydrogenase, N-methyl-D-aspartate receptor 2(NMDAr2) and phosphorylated N-methyl-D-aspartate receptor 2(PNMDAr2) were assayed by immunoblotting. Anxiety-like behavior increased in all treatment groups at the same time EMF increased anxiety induced by maternal stress in the EMF/S group. The stress group showed decreased serotonin and increased corticosterone levels. ELF-EMF elevated the PNMDAr2/NMDAr2 ratio and 24(S)-hydroxy cholesterol compared to the control group but did not change corticosterone. EMF did not restore changes induced by stress in behavioral and molecular tests. The results of the current study,

clarified that ELF-EMF can induce anxiety-like behavior which may be attributed to an increase in the PNMDAr2/NMDAr2 ratio and 24(S)-OHC in the hippocampus, and prenatal stress may contribute to anxiety via a decrease in serotonin and an increase in corticosterone in the hippocampus. We also found that anxiety-like behavior induced by maternal stress exposure, is exacerbated by electromagnetic fields radiation.

(E) Hosseini E, Kianifard D. Effect of prenatal stress and extremely low-frequency electromagnetic fields on anxiety-like behavior in female rats: With an emphasis on prefrontal cortex and hippocampus. Brain Behav 13(4):e2949, 2023. (AS, CE, MC, CC, BE, IX)

Objective: Prenatal stress (PS) is a problematic situation resulting in psychological implications such as social anxiety. Ubiquitous extremely low-frequency electromagnetic fields (ELF-EMF) have been confirmed as a potential physiological stressor; however, useful neuroregenerative effect of these types of electromagnetic fields has also frequently been reported. The aim of the present study was to survey the interaction of PS and ELF-EMF on anxiety-like behavior. **Method:** A total of 24 female rats 40 days of age were distributed into four groups of 6 rats each: control, stress (their mothers were exposed to stress), EMF (their mothers underwent to ELF-EMF), and EMF/stress (their mothers concurrently underwent to stress and ELF-EMF). The rats were assayed using elevated plus-maze and open field tests. **Results:** Expressions of the hippocampus GAP-43, BDNF, and caspase-3 (cas-3) were detected by immunohistochemistry in Cornu Ammonis 1 (CA1) and dentate gyrus (DG) of the hippocampus and prefrontal cortex (PFC). Anxiety-like behavior increased in all treatment groups. Rats in the EMF/stress group presented more serious anxiety-like behavior. In all treatment groups, upregulated expression of cas-3 was seen in PFC, DG, and CA1 and downregulated expression of BDNF and GAP-43 was seen in PFC and DG and the CA1. Histomorphological study showed vast neurodegenerative changes in the hippocampus and PFC. **Conclusion:** The results showed ,female rats that underwent PS or/and EMF exhibited critical anxiety-like behavior and this process may be attributed to neurodegeneration in PFC and DG of the hippocampus and possibly decreased synaptic plasticity so-called areas.

Hosseini SM, Farashi S, Bashirian S. Electromagnetic radiation therapy for Parkinson's disease tremor reduction- systematic reviews and Bayesian meta-analyses for comparing the effectiveness of electric, magnetic and light stimulation methods. J Neuroeng Rehabil 20(1):129, 2023.

Purpose: Tremor is one of the key characteristics of Parkinson's disease (PD), leading to physical disabilities and often showing limited responses to pharmacological treatments. To suppress tremors in PD patients, several types of non-invasive and non-pharmacological methods have been proposed so far. In the current systematic review, three electromagnetic-based radiation strategies including electrical stimulation, magnetic stimulation, and light stimulation methods were reviewed and compared. **Methods:** Major databases were searched to retrieve eligible studies. For the meta-analysis, a random-effect Bayesian framework was used. Also, heterogeneity between studies was assessed using I2 statistic, prediction interval, and tau2. Publication bias was assessed using funnel plot, and the effectiveness of methods for reducing tremor was compared using network Bayesian meta-analysis. **Results and conclusion:** Thirty-

one studies were found for qualitative analysis, and 16 studies were found for quantitative synthesis. Based on the suppression ratio, methods can be ordered as electrical stimulation, light therapy, and magnetic stimulation. Furthermore, the results showed that electrical and magnetic stimulation were more effective for tremor suppression at early stages of PD, while light therapy was found to be more effective during the later stages of PD.

(E) Houpt JA, Pittman DW**, Barranco** JM**, Brooks** EH**, Smith** JC. **Behavioral effects of high-strength static magnetic fields on rats. J Neurosci 23(4):1498-1505, 2003. (AS, AE, BE)**

Advances in magnetic resonance imaging are driving the development of more powerful and higher-resolution machines with high-strength static magnetic fields. The behavioral effects of high-strength magnetic fields are largely uncharacterized, although restraint within a 9.4 T magnetic field is sufficient to induce a conditioned taste aversion (CTA) and induce brainstem expression of c-Fos in rats. To determine whether the behavioral effects of static magnetic fields are dependent on field strength, duration of exposure, and orientation with the field, rats were restrained within the bore of 7 or 14 T superconducting magnets for variable durations. Behavioral effects were assessed by scoring locomotor activity after release from the magnetic field and measuring CTA acquisition after pairing intake of a palatable glucose and saccharin (G+S) solution with magnetic field exposure. Magnetic field exposure at either 7 or 14 T suppressed rearing and induced tight circling. The direction of the circling was dependent on the rat's orientation within the magnetic field: if exposed head-up, rats circled counterclockwise; if exposed head-down, rats circled clockwise. CTA was induced after three pairings of taste and 30 min of 7 T exposure or after a single pairing of G+S and 1 min of 14 T exposure. These results suggest that magnetic field exposure has graded effects on rat behavior. We hypothesize that restraint with high-strength magnetic fields causes vestibular stimulation resulting in locomotor circling and CTA acquisition.

(E) Houpt TA, Cassell JA, Riccardi C, Kwon B, Smith JC. Suppression of drinking by exposure to a high-strength static magnetic field. Physiol Behav 90(1):59-65, 2007. (AS, AE, BE)

High-strength static magnetic fields of 7 T and above have been shown to have both immediate and delayed effects on rodents, such as the induction of locomotor circling and the acquisition of conditioned taste aversions. In this study, the acute effects of magnet field exposure on drinking were examined. Exposure to a 14.1-T magnetic field for as little as 5 min significantly decreased the amount of a glucose and saccharin solution (G+S) consumed by water-deprived rats over 10 min. The decreased intake could be accounted for largely, but not entirely, by an increase in the latency of magnet-exposed rats to initiate drinking. When intake was measured for 10-60 min after the initiation of drinking, thus controlling for increased latency, magnet-exposed rats still consumed less G+S than sham-exposed rats. The increased latency was not due simply to an inability of magnet-exposed rats to reach the elevated sipper tube of the G+S bottle, providing rats with long tubes that could be reached without raising their heads normalized intake but latency was still increased. The increased latency and decreased intake appeared to be secondary to somatic effects of magnet exposure, however, because during intraoral infusions magnet-exposed rats consumed the same amount of G+S with the same latency to reject as sham-exposed

rats. The suppression of drinking by magnetic field exposure is consistent with the acute effects of other aversive stimuli, such as whole-body rotation, on short-term ingestion. These results add to the evidence that high-static strength magnetic fields can have behavioral effects on rodents.

(E) Houpt TA, Cassell JA, Hood A, DenBleyker M, Janowitz I, Mueller K, Ortega B, Smith JC. Repeated exposure attenuates the behavioral response of rats to static high magnetic fields. Physiol Behav 99(4):500-508, 2010. (AS, AE, BE)

Exposure of rats to high strength static magnetic fields of 7 T or above has behavioral effects such as the induction of locomotor circling, the suppression of rearing, and the acquisition of conditioned taste aversion (CTA). To determine if habituation occurs across magnetic field exposures, rats were pre-exposed two times to a 14 T static magnetic field for 30 min on two consecutive days; on the third day, rats were given access to a novel 0.125% saccharin prior to a third 30-min exposure to the 14 T magnetic field. Compared to sham-exposed rats, pre-exposed rats showed less locomotor circling and an attenuated CTA. Rearing was suppressed in all magnet-exposed groups regardless of pre-exposure, suggesting that the suppression of rearing is more sensitive than other behavioral responses to magnet exposure. Habituation was also observed when rats underwent pre-exposures at 2-3h intervals on a single day. Components of the habituation were also long-lasting; a diminished circling response was observed when rats were exposed to magnetic field 36 days after 2 pre-exposures. To control for possible effects of unconditioned stimulus pre-exposure, rats were also tested in a similar experimental design with two injections of LiCl prior to the pairing of saccharin with a third injection of LiCl. Pre-exposure to LiCl did not attenuate the LiCl-induced CTA, suggesting that 2 pre-exposures to an unconditioned stimulus are not sufficient to explain the habituation to magnet exposure. Because the effects of magnetic field exposure are dependent on an intact vestibular apparatus, and because the vestibular system can habituate to many forms of perturbation, habituation to magnetic field exposure is consistent with mediation of magnetic field effects by the vestibular system.

(E) Houpt TA, Carella L**, Gonzalez D, Janowitz I, Mueller** A**, Mueller** K**, Neth** B**, Smith** JC. **Behavioral effects on rats of motion within a high static magnetic field. Physiol Behav 102(3-4):338-346, 2011. (AS, AE, BE)**

Some human subjects report vestibular disturbances such as vertigo, apparent motion, and nausea around or within high strength MRI systems operating at 4 T to 9.4 T. These vestibular effects have been ascribed to the consequences of movement through the high magnetic field. We have previously found that exposure to magnetic fields above 7 T suppresses rearing, causes locomotor circling, and induces conditioned taste aversion (CTA) in rodents. The present experiments were designed to test the effects on rats of motion through the magnetic field of the 14.1 T superconducting magnet. In Experiment 1, we compared the effects of multiple rapid insertions and removals from the center of the magnet to the effects of continuous exposure. Repeated traversal of the magnetic field gradient with only momentary exposure to 14.1 T was sufficient to suppress rearing and induce a significant CTA. Repeated insertion and removal from the magnet, however, did not have a greater effect than a single 30-min exposure on either acute locomotor behavior or CTA acquisition. Prolonged exposure was required to induce locomotor circling. In the second series of experiments, we controlled the rate of insertion and removal by

means of an electric motor. Locomotor circling appeared to be dependent on the speed of insertion and removal, but the suppression of rearing and the acquisition of CTA were independent of speed of insertion and removal. In Experiment 3, we inserted rats into the center of the magnet and then rotated them about their rostral-caudal axis during a 30-min 14.1 T exposure. Rotation within the magnet did not modulate the behavioral effects of exposure. We conclude that, in rats, movement through the steep gradient of a high magnetic field has some behavioral effects, but sustained exposure to the homogenous center of the field is required for the full behavioral consequences.

(NE) Hoyer C, Vogt MA, Richter SH, Zaun G, Zahedi Y, Maderwald S, Ladd ME, Winterhager E, Grümmer R, Gass P. Repetitive exposure to a 7 Tesla static magnetic field of mice in utero does not cause alterations in basal emotional and cognitive behavior in adulthood. Reprod Toxicol 34(1):86-92, 2012. (AS, AE, BE)

In the past three decades, magnetic resonance imaging (MRI) has been increasingly used in obstetrics to aid diagnostics of maternal and fetal conditions and has generally been considered a safe imaging method. However, the development of higher-performance systems employing, for example, stronger fields to improve the technique's diagnostic potential, necessitates on-going safety evaluation. Rodent studies provide an excellent opportunity to investigate not only acute but also long-term effects of magnetic field exposure in a systematic manner, and a behavioral analysis might help to uncover subtler effects which might result from magnetic field exposure of the vulnerable developing brain. We conducted a comprehensive investigation of emotional and cognitive behavior in adult mice which had been repeatedly exposed to a 7 Tesla static magnetic field in utero. Using well-validated tests, we did not observe any adverse behavioral alterations regarding emotional behavior as well as spatial and emotional learning.

(E) Hu Y, Lai J, Wan B, Liu X, Zhang Y, Zhang J, Sun D, Ruan G, Liu E, Liu GP, Chen C, Wang DW. Long-term exposure to ELF-MF ameliorates cognitive deficits and attenuates tau hyperphosphorylation in 3xTg AD mice. Neurotoxicology. 53:290-300, 2016. (AS, CE, BE, CC, MA, ND)

Although numerous studies have reported the influence of extremely low frequency magnetic field (ELF-MF) exposure on human health, its effects on cognitive deficits in Alzheimer's disease (AD) have remained under debate. Moreover, the influence of ELF-MF on hyperphosphorylated tau, which is one of the most common pathological hallmarks of AD, has not been reported to date. Therefore, transgenic mice (3xTg) were used in the present study. 3xTg mice, which express an APP/PS1 mutation combined with a tau (P301L) mutation and that develop cognitive deficits at 6 months of age, were subjected to ELF-MF (50Hz, 500μT) exposure or sham exposure daily for 3 months. We discovered that ELF-MF exposure ameliorated cognitive deficits and increased synaptic proteins in 3xTg mice. The protective effects of ELF-MF exposure may have also been caused by the inhibition of apoptosis and/or decreased oxidative stress levels that were observed in the hippocampus tissues of treated mice. Furthermore, tau hyperphosphorylation was decreased in vivo because of ELF-MF exposure, and this decrease was induced by the inhibition of GSK3β and CDK5 activities and activation of PP2Ac. We are the first to report that exposure to ELF-MF can attenuate tau

phosphorylation. These findings suggest that ELF-MF exposure could act as a valid therapeutic strategy for ameliorating cognitive deficits and attenuating tau hyperphosphorylation in AD.

(E) Huang L, Sun X, Wang L,
Pei G, Wang Y, Zhang Q, Liang Z, Wang D, Fu C, He C, Wei Q. Enhanced effect of combining bone marrow mesenchymal stem cells (BMMSCs) and pulsed electromagnetic fields (PEMF) to promote recovery after spinal cord injury in mice. MedComm. 3:e160, 2022. (AS, CE, FC, MC, CC, MA)

Spinal cord injury (SCI) is a destructive traumatic disease of the central nervous system without satisfying therapy efficiency. Bone marrow mesenchymal stem cells (BMMSCs) therapy promotes the neurotrophic factors' secretion and axonal regeneration, thereby promoting recovery of SCI. Pulsed electromagnetic fields (PEMF) therapy has been proven to promote neural growth and regeneration. Both BMMSCs and PEMF have shown curative effects for SCI; PEMF can further promote stem cell differentiation. Thus, we explored the combined effects of BMMSCs and PEMF and the potential interaction between these two therapies in SCI. Compared with the SCI control, BMMSCs, and PEMF groups, the combinational therapy displayed the best therapeutic effect. Combinational therapy increased the expression levels of nutritional factors including brain-derived neurotrophic factor (BDNF), nerve growth factors (NGF) and vascular endothelial growth factor (VEGF), enhanced neuron preservation (NeuN and NF-200), and increased axonal growth (MBP and myelin sheath). Additionally, PEMF promoted the expression levels of BDNF and VEGF in BMMSCs via Wnt/β-catenin signaling pathway. In summary, the combined therapy of BMMSCs and PEMF displayed a more satisfactory effect than BMMSCs and PEMF therapy alone, indicating a promising application of combined therapy for the therapy of SCI.

(E) Hui Y, Sun C, Yang Q, Liu G, Yuan T, He P, Qin X. Magnetic Field-Driven Electrogenic Scaffold Enhances the Nerve Regeneration. Artif Organs. 2025 Dec 1. doi: 10.1111/aor.70065. Epub ahead of print. PMID: 41321258. (AS, CE, MC, MA)

Background: Neural conduits (NGCs) are widely used for peripheral nerve regeneration but have shown limited therapeutic effects. Electrical stimulation combined with NGCs is becoming a new treatment paradigm. Conventional electrical stimulation approaches for nerve regeneration are typically hindered by inconvenience, infection, and may cause secondary damage. **Methods:** This study developed a non-contact electrical stimulation platform using a magnetic field-coupled polycaprolactone/conductive polymer poly(3,4-ethylenedioxythiophene)/black phosphorus nerve conduit. This composite nerve conduit exhibited excellent electrical properties and biocompatibility. When placed in an external rotating magnetic field, it was able to transmit pulsed currents into the targeted sites due to electromagnetic induction. **Results:** The regeneration levels achieved with the magnetic field-driven nerve conduit were comparable to those of autologous transplantation. Immunofluorescence and histochemistry results demonstrated that this magnetic field-driven nerve conduit enhances axonal regeneration, neovascularization, and inflammation regulation. **Conclusion:** This work opens a new avenue

for low-invasive and high-security bioelectronic therapy for long-segment peripheral nerve defects, with potential applications in various tissue regeneration engineering.

(E) Hung CS, Anderson C, Horne JA, McEvoy P. Mobile phone 'talk-mode' signal delays EEG-determined sleep onset. Neurosci Lett. 421(1):82-86, 2007. (HU, AE, EE, BE)

Mobile phones signals are pulse-modulated microwaves, and EEG studies suggest that the extremely low-frequency (ELF) pulse modulation has sleep effects. However, 'talk', 'listen' and 'standby' modes differ in the ELF (2, 8, and 217Hz) spectral components and specific absorption rates, but no sleep study has differentiated these modes. We used a GSM900 mobile phone controlled by a base-station simulator and a test SIM card to simulate these three specific modes, transmitted at 12.5% (23dBm) of maximum power. At weekly intervals, 10 healthy young adults, sleep restricted to 6h, were randomly and single-blind exposed to one of: talk, listen, standby and sham (nil signal) modes, for 30 min, at 13:30 h, whilst lying in a sound-proof, lit bedroom, with a thermally insulated silent phone beside the right ear. Bipolar EEGs were recorded continuously, and subjective ratings of sleepiness obtained every 3 min (before, during and after exposure). After exposure the phone and base-station were switched off, the bedroom darkened, and a 90 min sleep opportunity followed. We report on sleep onset using: (i) visually scored latency to onset of stage 2 sleep, (ii) EEG power spectral analysis. There was no condition effect for subjective sleepiness. Post-exposure, sleep latency after talk mode was markedly and significantly delayed beyond listen and sham modes. This condition effect over time was also quite evident in 1-4Hz EEG frontal power, which is a frequency range particularly sensitive to sleep onset. It is possible that 2, 8, 217Hz modulation may differentially affect sleep onset.

(E) Isaković J, Slatković F, Jagečić D, Petrović DJ, Mitrečić D. Pulsating Extremely Low-Frequency Electromagnetic Fields Influence Differentiation of Mouse Neural Stem Cells towards Astrocyte-like Phenotypes: In Vitro Pilot Study. Int J Mol Sci 25(7):4038, 2024. (CS, AE, MC, CC, MA)

Even though electromagnetic fields have been reported to assist endogenous neurogenesis, little is known about the exact mechanisms of their action. In this pilot study, we investigated the effects of pulsating extremely low-frequency electromagnetic fields on neural stem cell differentiation towards specific phenotypes, such as neurons and astrocytes. Neural stem cells isolated from the telencephalic wall of B6(Cg)-Tyrc-2J/J mouse embryos (E14.5) were randomly divided into three experimental groups and three controls. Electromagnetic field application setup included a solenoid placed within an incubator. Each of the experimental groups was exposed to 50Hz ELF-EMFs of varied strengths for 1 h. The expression of each marker (NES, GFAP, β-3 tubulin) was then assessed by immunocytochemistry. The application of high-strength ELF-EMF significantly increased and low-strength ELF-EMF decreased the expression of GFAP. A similar pattern was observed for β-3 tubulin, with high-strength ELF-EMFs significantly increasing the immunoreactivity of β-3 tubulin and medium- and low-strength ELF-EMFs decreasing it. Changes in NES expression were observed for medium-strength ELF-EMFs, with a demonstrated significant upregulation. This suggests that, even though ELF-EMFs

appear to inhibit or promote the differentiation of neural stem cells into neurons or astrocytes, this effect highly depends on the strength and frequency of the fields as well as the duration of their application. While numerous studies have demonstrated the capacity of EMFs to guide the differentiation of NSCs into neuron-like cells or β-3 tubulin+ neurons, this is the first study to suggest that ELF-EMFs may also steer NSC differentiation towards astrocyte-like phenotypes.

(E) Ilić AŽ, de Luka SR, Popović TB, Debeljak-Martačić J, Kojadinović M, Ćirković S, Ristić-Djurović JL, Trbovich AM. Distinct fatty acid redistribution and textural changes in the brain tissue upon the static magnetic field exposure. Environ Toxicol Pharmacol. 19:103853, 2022. (AS, CE, CC)

We observed different outcomes upon the subacute exposure to the 128 mT highly homogeneous static magnetic field (SMF) when its orientation was (i) aligned with the vertical component of the geomagnetic field; (ii) in the opposite direction. We employed the fatty acids (FA) composition and digital image analyses (DIA) to provide insights into the underlying processes and examine the possible weak SMF effects. Swiss-Webster male mice were whole-body exposed for 1h/day over five days. Brain tissue's thin liquid chromatography resulted in brain FA composition, indicating a possible sequence of changes due to the SMF exposure. Quantitative DIA accurately assessed different image parameters. Delicate textural changes were revealed in the group where pathohistological or biochemical alterations have not been detected. DIA-based biological markers seem to be very promising for studying delicate tissue changes, which results from the high sensitivity and wide availability of DIA. We observed different outcomes upon the subacute exposure to the 128 mT highly homogeneous static magnetic field (SMF) when its orientation was (i) aligned with the vertical component of the geomagnetic field; (ii) in the opposite direction. We employed the fatty acids (FA) composition and digital image analyses (DIA) to provide insights into the underlying processes and examine the possible weak SMF effects. Swiss-Webster male mice were whole-body exposed for 1h/day over five days. Brain tissue's thin liquid chromatography resulted in brain FA composition, indicating a possible sequence of changes due to the SMF exposure. Quantitative DIA accurately assessed different image parameters. Delicate textural changes were revealed in the group where pathohistological or biochemical alterations have not been detected. DIA-based biological markers seem to be very promising for studying delicate tissue changes, which results from the high sensitivity and wide availability of DIA.

(E) Ishay JS, Plotkin M, Volynchik S, Shaked M, Schuss Z, Bergman DJ. Exposure to an additional alternating magnetic field affects comb building by worker hornets. Physiol Chem Phys Med NMR. 39(1):83-88, 2007. (AS, CE, BE)

Oriental hornet workers, kept in an Artificial Breeding Box (ABB) without a queen, construct within a few days brood combs of hexagonal cells with apertures facing down. These combs possess stems that fasten the former to the roof of the ABB. In an ABB with adult workers (more than 24 h after eclosion), exposed to an AC (50 Hz) magnetic field of a magnitude of B = 50-70 mGauss, the combs and cells are built differently from those of a control ABB, subjected only to the natural terrestrial magnetic field. The effects of the additional magnetic field consist of (a) 35-55% smaller number of cells and fewer eggs in each comb, (b) disrupted symmetry of

building, with many deformed and imperfectly hexagonal cells, and (c) more delicate and slender comb stems.

(E) Jadidi M, Firoozabadi SM, Rashidy-Pour A, Sajadi AA, Sadeghi H, Taherian AA. Acute exposure to a 50 Hz magnetic field impairs consolidation of spatial memory in rats. Neurobiol Learn Mem. 88(4):387-392, 2007. (AS, CE, BE)

This study was planned to evaluate the effect of an exposure to magnetic fields on consolidation and retrieval of hippocampus dependent spatial memory using a water maze. In Experiments 1 and 2, rats were trained in a hidden version (spatial) of water maze task with two blocks of four trials. The retention of spatial memory was evaluated 48 h later. Exposure to a 50 Hz 8 mT, but not 2 mT magnetic fields for 20 min immediately after training impaired retention performance. The same time exposure shortly before retention testing had no effect. In Experiment 3, rats were trained in a cued version of water maze with two blocks of four trials. Exposure to magnetic field at 8 mT for 20 min immediately after training did not impair retention performance. These findings indicate that acute exposure to a 50 Hz magnetic field at 8 mT for short time can impair consolidation of spatial memory.

(E) Jadidi M, Khatami MS, Mohammad-Pour F, Afsaneh Bandavi A, Rashidy-Pour A, Vafaei AA, Taherian AA, Miladi-Gorji H. Effects of extremely low frequency magnetic field on the development of tolerance to the analgesic effect of morphine in rats. Bioelectromagnetics. 38:618-625, 2017. (AS, AE, BE, MA)

This study examined the effects of low frequency magnetic field (MF) on tolerance to analgesic effect of morphine in rats. Rats were made tolerant to morphine by injecting morphine (10 mg/kg, s) once daily for 8 consecutive days. Rats were simultaneously exposed to an MF (50 Hz at 1, 50, and 100 μT for 30 min) before, immediately, or 30 min after injection of morphine, and also exposed to a 0.5, 6, 12, and 30 Hz at 100 μT for 30 min before injection of morphine. The percentage of maximum possible effect of morphine (% MPE) was measured on the 1st, 4th, and 8th days by hot plate test. We observed that MF radiation (50 Hz at 1 μT and 30 Hz at 100 μT) immediately before and MF radiation (50 Hz at 100 μT) after morphine injection prevented the development of morphine tolerance compared to control. Also, we found that exposure to MF (50 Hz at 1, 50, and 100 μT) 30 min after injection of morphine failed to maintain the analgesic effect of morphine. Our results showed that exposure to low frequency electromagnetic field (30 and 50 Hz) immediately before or after the injection of morphine may be a potential method for treating the development of morphine tolerance in rats.

(E) Jadidi T, Asadian N, Jadidi M, Vafaei AA. EMF promote BMSCs differentiation and functional recovery in hemiparkinsonian rats. Neurosci Lett 784:136765, 2022. (CS, AS, CE, BE, MC, MA, ND)

Bone marrow mesenchymal stem cells (BMSCs) have self-renewal ability while maintaining the proliferation facility. The BMSCs reproducing ability could affect by electromagnetic fields (EMFs) as a physical inducing factor. We focused on the EMF (400 μT, 75 Hz) exposed multi-potential BMSCs which differentiated and successfully implanted in the substantia nigra pars

compacta (SNpc) of Parkinson's disease rat model. The purified BMSCs are exposed to sinusoidal and square waveform EMF (1h/1 week or 7h/1 day) then injected into the left SNpc of Parkinson's rats. To evaluate the morphology of EMF exposed BMSCs, the cresyl violet staining labeled the Nissl bodies. After evaluation of the rat's activity by behavioral tests (open-field and rotarod tests), the brains were obtained for the preparation of SNpc blocks and carry out the cresyl violet staining. Cell morphology proved most cell differentiation to neurons in the sinusoidal EMF groups. In the sinusoidal EMF exposure groups, large and small neurons were seen with apparent synapses. Although in the square EMF exposed groups some neurons were seen, most of the differentiated cells were astrocytes, microglia, and oligodendrocyte. The results confirmed an improvement in locomotors' activity of BMSC alone and sinusoidal EMF exposed groups. We presented a low-frequency EMF (75 Hz) to promote the capability of BMSC proliferation, differentiation to neurons and glial cells, and motor coordination activity in the treatment of hemiparkinsonian rats.

(E) Jakubowska M, Urban-Malinga B, Otremba Z, Andrulewicz E. Effect of low frequency electromagnetic field on the behavior and bioenergetics of the polychaete Hediste diversicolor. Marine Environ Res. 150:104766, 2019. (AS, CE, FC, BE)

The aim of the present study was to determine the effect of an electromagnetic field (EMF) of value typically recorded in the vicinity of submarine cables (50 Hz, 1 mT) on the behavior and bioenergetics of the polychaete Hediste diversicolor. No avoidance or attraction behavior to EMF was shown, but the burrowing activity of H. diversicolor was enhanced in EMF treatment, indicating a stimulating effect on bioturbation potential. The polychaete maintained a positive energy balance and high amount (85% of assimilated energy) of energy available for individual production (scope for growth) after exposure to EMF. Food consumption and respiration rates were not affected but ammonia excretion rate was significantly reduced in EMF-exposed animals compared to the control conditions (geomagnetic field). The mechanisms behind this effect remain, however, unclear. This is the first study demonstrating the effects of environmentally realistic EMF value on the behavior and physiology of marine invertebrates, thus there is a need for more research.

(E) Janać B, Tovilović G, Tomić M, Prolić Z, Radenović L. Effect of continuous exposure to alternating magnetic field (50 Hz, 0.5 mT) on serotonin and dopamine receptors activity in rat brain. Gen Physiol Biophys. 28 Spec No:41-46, 2009. (AS, CE, FC)

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.

(E) Janać B, Selaković V, Rauš S, Radenović L, Zrnić M, Prolić Z. Temporal patterns of extremely low frequency magnetic field-induced motor behavior changes in Mongolian gerbils of different age. Int J Radiat Biol. 88(4):359-366, 2012. (AS, CE, BE)

PURPOSE: The aim of this study was to investigate the influence of extremely low frequency magnetic field (ELF-MF) on different behavior parameters (locomotion, stereotypy, and immobility) in 3- and 10-month-old male Mongolian gerbils. MATERIALS AND METHODS: The animals were continuously exposed to ELF-MF (50 Hz; 0.1, 0.25 and 0.5 mT) for seven days. Their behavior was monitored for 60 min in the open field after the 1st, 2nd, 4th, and 7th day of exposure (immediate effect), and three days after ELF-MF exposure had been ceased (delayed effect). RESULTS: In 3-month-old gerbils, exposure to ELF-MF (0.1, 0.25 and 0.5 mT) increased motor behavior (locomotion and stereotypy), and consequently decreased immobility. Additionally, ELF-MF had delayed effect (except 0.25 mT) on stereotypy and immobility. In 10-month-old gerbils, ELF-MF of 0.1, 0.25 and 0.5 mT induced decrease, slight increase, and pronounced stimulation of motor behavior, respectively. Regardless of magnetic induction value, increased motor behavior was observed three days after ELF-MF exposure has been ceased (delayed effect). CONCLUSIONS: It can be proposed that the specific temporal patterns of ELF-MF-induced motor behavior changes in 3- and 10-month-old gerbils are a consequence of age-dependent morpho-functional differences in the brain structures responsible for a control of motor behavior.

(E) Jankowska M, Pawlowska-Mainville A, Stankiewicz M, Rogalska J, Wyszkowska J. Exposure to 50 Hz electromagnetic field changes the efficiency of the scorpion alpha toxin. J Venom Anim Toxins Incl Trop Dis. 21:38, 2015. (AS, CS, AE, FC)

BACKGROUND: Extremely low-frequency (50 Hz) electromagnetic field (ELF-EMF) is produced by electric power transmission lines and electronic devices of everyday use. Some phenomena are proposed as "first effects" of ELF-EMF: the discrete changes in the membrane potential and the increase of the calcium channel activity as well as the intracellular concentration of Ca(2+). Interaction of the scorpion alpha toxin with the sodium channel depends on the orientation of the charges and may be perturbed by changes in the membrane polarization. The toxin induces overexcitability in the nervous system and an increase in the neurotransmitters released with different consequences, mainly the paralysis of muscles. We assumed that the exposure to ELF-EMF 0.7 mT will change the effects of the insect selective scorpion alpha toxin (recombinant LqhαIT from Leiurus quinquestriatus hebraeus) at the level of the cercal nerve function, the synaptic transmission and on the level of entire insect organism. Taking into account the compensatory mechanisms in organisms, we tested in addition ten times higher ELF-EMF on whole insects. METHODS: Experiments were performed in vivo on cockroaches (Periplaneta americana) and in vitro - on isolated cockroach abdominal nerve cord with cerci. In biotests, the effects of LqhαIT (10(-8) M) were estimated on the basis of the insect ability to turn

back from dorsal to ventral side. Three groups were compared: the control one and the two exposed to ELF-EMF - 0.7 and 7 mT. Bioelectrical activity of the cercal nerve and of the connective nerve that leaves the terminal abdominal ganglion was recorded using extracellular electrodes. LqhαIT (5 × 10(-8) M) induced modifications of neuronal activity that were observed in the control cockroach preparations and in the ones exposed to ELF-EMF (0.7 mT). The exposure to ELF-EMF was carried out using coils with a size appropriate to the examined objects. RESULTS: The exposure to ELF-EMF (0.7 mT) modified the effects of LqhαIT (5 × 10(-8) M) on activity of the cercal nerve and of the connective nerve. We observed a decrease of the toxin effect on the cercal nerve activity, but the toxic effect of LqhαIT on the connective nerve was increased. Biotests showed that toxicity of LqhαIT (10(-8) M) on cockroaches was reduced by the exposure to ELF-EMF (0.7 and 7 mT). CONCLUSIONS: The exposure to 50 Hz ELF-EMF modified the mode of action of the anti-insect scorpion alpha toxin LqhαIT at cellular level of the cockroach nervous system and in biotests. Toxin appeared as a usefull tool in distinguishing between the primary and the secondary effects of ELF-EMF.

(E) Jankowska M, Klimek A, Valsecchi C, Stankiewicz M, Wyszkowska J, Rogalska J. Electromagnetic field and TGF-β enhance the compensatory plasticity after sensory nerve injury in cockroach Periplaneta americana. Sci Rep 11(1):6582, 2012. (AS, CE, FC, MA, IX)

Recovery of function after sensory nerves injury involves compensatory plasticity, which can be observed in invertebrates. The aim of the study was the evaluation of compensatory plasticity in the cockroach (Periplaneta americana) nervous system after the sensory nerve injury and assessment of the effect of electromagnetic field exposure (EMF, 50 Hz, 7 mT) and TGF-β on this process. The bioelectrical activities of nerves (pre-and post-synaptic parts of the sensory path) were recorded under wind stimulation of the cerci before and after right cercus ablation and in insects exposed to EMF and treated with TGF-β. Ablation of the right cercus caused an increase of activity of the left presynaptic part of the sensory path. Exposure to EMF and TGF-β induced an increase of activity in both parts of the sensory path. This suggests strengthening effects of EMF and TGF-β on the insect ability to recognize stimuli after one cercus ablation. Data from locomotor tests proved electrophysiological results. The takeover of the function of one cercus by the second one proves the existence of compensatory plasticity in the cockroach escape system, which makes it a good model for studying compensatory plasticity. We recommend further research on EMF as a useful factor in neurorehabilitation.

(E) Jin Z, Dong L, Tian L, Zhou M, Zheng Y. Regulation of LTP at rat hippocampal Schaffer-CA1 *in vitro* by musical rhythmic magnetic fields generated by red-pink (soothing) music tracks. Int J Radiat Biol 99(3):439-445, 2023.(CS, AE, EE)

Purpose: Music therapy, like red-pink (soothing) music, is an important treatment for neurological disorders associated with learning and memory. Magnetic fields have been proved to have a similar regulating effect. However, the effect of magnetic fields with musical rhythm generated by the combination of the two has not been confirmed. This study aimed to investigate the regulation of magnetic stimulation with music rhythm on LTP (long-term potentiation) of Schaffer-CA1. **Materials and methods:** This article selected three sorts of music tracks in different frequencies (music track 1 *Turkish March*, music track 2 *Moonlight Sonata*, music track 3 *Funeral March*) and four sorts of pure sinusoidal tracks of four different harmonic frequency

(music track 4: the frequency is 3500 Hz; music track 5: the frequency is 2500 Hz; music track 6: the frequency is 1500 Hz; music track 7: the frequency is 500 Hz). These music tracks are converted into analog signals by the external sound card and power amplifier and fed into a homemade coil that meets the demand for this frequency bandwidth. The coil can generate seven sorts of time-varying magnetic fields with musical rhythm with a mean intensity of about 2 mT. We used multi-electrode array (MEA) to record the LTP signals of Schaffer-CA1 synaptic induced by seven sorts of musical rhythmic magnetic fields and analyze the regulation of them. **Results:** The musical rhythmic magnetic fields generated by track 1 and track 2 have a remarkable enhancing effect on the amplitude of fEPSPs (field excitatory postsynaptic potentials) *($p < 0.05$)*, and these effects intensify with the increase of frequency. Nevertheless, there is no significant enhancing effect on LTP of the rhythmic magnetic field generated by track 3 *($p > 0.05$)*. The sinusoidal magnetic fields generated by track 4 and track 5 have an enhancing effect on the amplitude of fEPSPs *($p < 0.05$)*, and the enhancement is better than track 1 and track 2. The sinusoidal magnetic fields generated by track 6 and track 7 have an inhibiting effect *($p < 0.05$)*. **Conclusion:** We found that the enhancing effect of musical rhythmic magnetic fields generated by track 1 was the most significant. The frequency of 1500 Hz could be a turning-point frequency in the regulation of magnetic field on LTP.

(E) Kakikawa M, Kenmochi A, Yamada S. Effect of 60 Hz magnetic fields on social feeding behavior of *npr-1* receptor mutants in *Caenorhabditis elegans*. Electromagn Biol Med. 2025 Jun 26:1-9. doi: 10.1080/15368378.2025.2523773. Epub ahead of print. (AS, AE, BE)

Previous studies indicated that magnetic fields (MF) could alter the conformation of membrane proteins such as some drug influx transporters and affect their function. In this study, we focused on two mutants of *npr-1* receptor gene related to feeding behavior in *Caenorhabditis elegans* (*C. elegans)* to investigate the effect of 60 Hz, 50 mT MF on a receptor in neurotransmission. The wild-type laboratory strain Bristol N2 in *C. elegans* forages solitary on the *E. coli* lawn, whereas *npr-1* mutant of N2 aggregate on food and take on social feeding behavior because of its altered function. Under MF exposure, the number of aggregates exhibiting social feeding behavior on two mutants, IM222 and DA609, was decreased by 40% and 25%, respectively. Meanwhile, *npr-1* is not involved in the behavior to attractant diacetyl in *C. elegans*, and the moving speed and reach rate to attractant in two mutants was not affected by MF exposure for up to 90 min. The results indicate that MF can affect the altered function of NPR-1 in mutant strains and partially change the feeding behaviour of the *npr-1* mutants from social to solitary. Furthermore, considering the position of these amino acid substitutions in NPR-1 mutant receptors, the extracellular parts of membrane protein may be more affected by MF than the transmembrane part.

(E) Kaneda E, Kawai T, Okamura Y, Miyagawa S. Effects of moderate static magnetic fields on voltage-gated potassium ion channels in sympathetic neuron-like PC12 cells. Physiol Rep. 13(6):e70236, 2025. (CS, AE, EE)

While exposure of moderate static magnetic fields (SMF) can alter neuronal excitability, the effects on sympathetic neurons remain underexplored. This study investigates the effects of moderate SMF on Kv channels in the plasma membrane of sympathetic neuron-like PC12 cells. The current density of Kv channels was significantly lower in the 18-h magnet-exposed group, with effects persisting even after the

magnet was removed before patch-clamp measurements. The current density of outward current in the presence of TEA was not different between the two groups, indicating that magnetic field affects TEA-sensitive Kv channels. To further explore these changes, RNA sequencing was performed on samples from both the Sham and 18-h magnet-exposed groups, identifying 37 moderate SMF-sensitive genes. Changes in mRNA expression levels and KEGG analysis suggested that pathways involved in the inhibition of neuronal excitability, such as GABAB receptor activation and Kir3 channel opening, may be more likely to be activated. In conclusion, moderate SMF is strongly associated with reduced current density in PC12 cells, particularly affecting Kv channels. The present study provides fundamental information on the influence of long-term SMF exposure on the excitability of sympathetic neurons.

(E) Kantar Gok D, Akpinar D, Yargicoglu P, Ozen S, Aslan M, Demir N, Derin N, Agar A. Effects of extremely low-frequency electric fields at different intensities and exposure durations on mismatch negativity. Neuroscience. 272C:154-166, 2014. (EE, AS, CE, EE, OX)

The effects of extremely low-frequency electric fields (ELF-EFs, 3-300Hz) on lipid peroxidation levels and antioxidant enzyme activities have been shown in many tissues and plasma after exposure to 50-Hz alternating current (AC) electric fields. However, similar studies investigating brain lipid peroxidation status are limited. Moreover and as far as we know, no study has been conducted to examine mismatch negativity (MMN) response in rats following exposure to a 50-Hz AC electric field. Therefore, the purpose of the study was to investigate different intensities and exposure durations of ELF-EFs on MMN component of event-related potentials (ERPs) as well as apoptosis and oxidative brain damage in rats. Ninety male rats, aged 3months were used in our study. A total of six groups, composed of 15 animals each, was formed as follows: sham-exposed rats for 2weeks (C2), sham-exposed rats for 4weeks (C4), rats exposed to 12-kV/m and 18-kV/m electric fields for 2weeks (E12-2 and E18-2), rats exposed to 12- and 18-kV/m electric fields for 4weeks (E12-4 and E18-4). At the end of the experimental period, MMN responses were recorded in urethane-anesthetized rats by electrodes positioned stereotaxically to the surface of the dura. After MMN recordings, animals were killed by exsanguination and their brain tissues were removed for 4-hydroxy-2-nonenal (4-HNE), protein carbonyl and TUNEL analysis. In the current study, different change patterns in ERP parameters were observed dependent on the intensity and exposure duration of ELF-EFs. There were differences in the amplitudes of ERP between the responses to the standard and the deviant tones in all groups. When peak-to-peak amplitude of the difference curves was evaluated, MMN amplitude was significantly decreased in the E18-4 group compared with the C4 group. Additionally, the amount of 4-HNE was increased in all experimental groups compared with the control group. Consequently, it could be concluded that electric field decreased MMN amplitudes possibly induced by lipid peroxidation.

(E) Kantar D, Acun AD, Er H, Afsar E, Yargıcoglu P. Anxiolytic-Like Effects of Extremely Low Frequency Electric Field in Stressed Rats: Involvement of 5-HT2C Receptors. Int. J. Rad. Biol. 99(9):1473-1482, 2023. (AS, AE, CC, BE, EF)

Background. Possible modulatory effects of non-invasive brain stimulation have gained interest recently. In our study, the effect of low frequency electric fields (LF-EF) on stress-induced electrophysiological, behavioral changes and the possible involvement of serotonergic 5-HT2C receptors were investigated. **Materials and Methods**. A total of 8 groups including the control

groups were formed by applying LF-EF with or without a 5-HT2C receptor agonist to naïve or acute stress exposed rats to demonstrate the effects of LF-EF. LF-EF administration at 10 kV/m was started 30 minutes before acute stress application and lasted for 1 hour in total. Anxiety levels and social interaction were evaluated using the elevated plus maze test and social interaction test, respectively. Auditory evoked potentials (AEP) were recorded by using ascending loudness paradigms. Loudness dependence AEP (LDAEP) was calculated by using amplitude values to analyze serotonergic transmission. Serotonin and glucocorticoid levels were measured in the frontal cortex and hippocampus. **Results** It was observed that the applied LF-EF reduced the anxiety behavior, and attenuated the LDAEP responses in stress and/or 5-HT2C receptor agonist applied groups. In parallel, an increase in serotonin levels and a decrease in glucocorticoid levels were observed. However, LF-EF exposure was ineffective in impaired social interaction**. Conclusions** Our findings show that 10 kV/m LF-EF administration may modulate the neural network and physiological responses associated with mild acute stress. 5-HT2C receptor dependent functions are thought to play a role in the anxiolytic effect of LF-EF.

(E) Kapri-Pardes E, Hanoch T, Maik-Rachline G, Murbach M, Bounds PL, Kuster N, Seger R. Activation of Signaling Cascades by Weak Extremely Low Frequency Electromagnetic Fields. Cell Physiol Biochem. 43:1533-1546, 2017. (CS, AE, CC, OX)

Results from recent studies suggest that extremely low frequency magnetic fields (ELF-MF) interfere with intracellular signaling pathways related to proliferative control. The mitogen-activated protein kinases (MAPKs), central signaling components that regulate essentially all stimulated cellular processes, include the extracellular signal-regulated kinases 1/2 (ERK1/2) that are extremely sensitive to extracellular cues. Anti-phospho-ERK antibodies serve as a readout for ERK1/2 activation and are able to detect minute changes in ERK stimulation. The objective of this study was to explore whether activation of ERK1/2 and other signaling cascades can be used as a readout for responses of a variety of cell types, both transformed and non-transformed, to ELF-MF. METHODS: We applied ELF-MF at various field strengths and time periods to eight different cell types with an exposure system housed in a tissue culture incubator and followed the phosphorylation of MAPKs and Akt by western blotting. RESULTS: We found that the phosphorylation of ERK1/2 is increased in response to ELF-MF. However, the phosphorylation of ERK1/2 is likely too low to induce ELF-MF-dependent proliferation or oncogenic transformation. The p38 MAPK was very slightly phosphorylated, but JNK or Akt were not. The effect on ERK1/2 was detected for exposures to ELF-MF strengths as low as 0.15 µT and was maximal at ~10 µT. We also show that ERK1/2 phosphorylation is blocked by the flavoprotein inhibitor diphenyleneiodonium, indicating that the response to ELF-MF may be exerted via NADP oxidase similar to the phosphorylation of ERK1/2 in response to microwave radiation. CONCLUSIONS: Our results further indicate that cells are responsive to ELF-MF at field strengths much lower than previously suspected and that the effect may be mediated by NADP oxidase. However, the small increase in ERK1/2 phosphorylation is probably insufficient to affect proliferation and oncogenic transformation. Therefore, the results cannot be regarded as proof of the involvement of ELF-MF in cancer in general or childhood leukemia in particular.

(E) Karimi AS, Salehi I, Shykhi T, Zare S, Komaki A. Effects of exposure to extremely low-frequency electromagnetic fields on spatial and passive avoidance learning and memory, anxiety-like behavior and oxidative stress in male rats. Behav Brain Res 359:630-638, 2019.(AS, CE, BE, OX)

There are many controversies about the safety of extremely low-frequency electromagnetic field (ELF-EMF) on body health and cognitive performance. In the present study, we explored the effects of ELF-EMF on oxidative stress and behaviors of rats. Seventy-two adult male Wistar rats were randomly divided into following groups, control, sham exposure group and the ELF-EMF exposure groups (1 μT, 100 μT, 500 μT, and 2000 μT). After 60 days exposure (2 h/day), elevated plus maze (EPM), Morris water maze (MWM) and Passive avoidance learning (PAL) tasks were used to evaluate the anxiety-like behavior, spatial and passive learning and memory, respectively. Some days after behavioral examination, oxidative stress markers were measured. During spatial reference memory test, animals in ELF-EMF exposure groups (100, and 2000 μT) spent more time in target zone ($F(4, 55) = 5.699$, $P = 0.0007$, One-way ANOVA). In PAL retention, the step through latency in the retention test (STLr) in ELF-EMF exposure groups (100,500, and 2000 μT) was significantly greater than control group ($F(4, 55) = 29.13$, $P < 0.0001$, One-way ANOVA). In EPM test, ELF-EMF exposure (500 and 2000 μT) decreased the percentage of the entries into the open arms ($F(4, 55) = 26.31$, $P < 0.0001$, one-way ANOVA). ELF-EMF exposure (100, and 500 μT) increased Malondialdehyde (MDA) concentration ($F(4, 25) = 79.83$, $P < 0.0001$, One-way ANOVA). Our results may allow the conclusion that exposure to ELF-EMFs can improve memory retention (but not acquisition) in the adult male rats. Although exposure to ELF-EMFs could be a factor in the development of anxious state or oxidative stress.

(E) Kaur S, Jain S, Bhardwaj R, Kumaran SS, Kochhar KP. Modulation of the biphasic pattern of cortical reorganization in spinal cord-transected rats by external magnetic fields. J Biosci.50:71, 2025. (AS, CE, MC, BE, EE, MA)

A biphasic pattern of reorganization in the somatosensory cortical area, representing the hindlimb or forelimb, has been shown after complete spinal cord injury (cSCI) in rats. The present study hypothesized that extremely low-frequency magnetic fields (ELF-MF) would favourably modulate this biphasic pattern of cortical plasticity by altering brain-derived neurotrophic factor (BDNF) and neurite outgrowth inhibitor A (isoform of reticulon- 4) (Nogo-A) levels, leading to functional and electrophysiological recovery in cSCI rats. Adult male Wistar rats underwent cSCI at the T-13 spinal level, followed by ELF-MF exposure for either 5, 12, or 32 days, for analysis of the biphasic pattern. A set of motor and sensorimotor behavioural tests, spinal cord lesion volume, cortical electroencephalography (EEG), expression of neurotrophic factor (BDNF), and inhibitory molecule (Nogo-A) were recorded at each time period. Significant ($p \leq 0.01$) recovery was evident in the Basso-Beattie- Bresnahan (BBB) locomotor score, allodynia, grip strength, power spectrum of EEG waves, and lesion volume after 32 days of ELF-MF. Although both SCI and SCI+MF rats exhibited characteristic biphasic patterns in the expression of Nogo-A and BDNF, the SCI+MF group showed a significant increase in BDNF levels along with a decrease in Nogo-A. These findings suggest that ELF-MF enhances functional recovery after cSCI by moderating molecular and electrophysiological markers of cortical plasticity, without disrupting the inherent biphasic expression dynamics.

(E) Kawasaki H, Okano H, Nedachi T, Nakagawa-Yagi Y, Hara A, Ishida N Effects of an electric field on sleep quality and life span mediated by ultraviolet (UV)-A/blue light photoreceptor CRYPTOCHROME in Drosophila. Sci Rep 11(1):20543, 2021. (AS, CE, BE, EF)

Although electric fields (EF) exert beneficial effects on animal wound healing, differentiation, cancers and rheumatoid arthritis, the molecular mechanisms of these effects have remained unclear about a half century. Therefore, we aimed to elucidate the molecular mechanisms underlying EF effects in Drosophila melanogaster as a genetic animal model. Here we show that the sleep quality of wild type (WT) flies was improved by exposure to a 50-Hz (35 kV/m) constant electric field during the day time, but not during the night time. The effect was undetectable in cryptochrome mutant (cry^b) flies. Exposure to a 50-Hz electric field under low nutrient conditions elongated the lifespan of male and female WT flies by ~ 18%, but not of several cry mutants and cry RNAi strains. Metabolome analysis indicated that the adenosine triphosphate (ATP) content was higher in intact WT than cry gene mutant strains exposed to an electric field. A putative magnetoreceptor protein and UV-A/blue light photoreceptor, CRYPTOCHROME (CRY) is involved in electric field (EF) receptors in animals. The present findings constitute hitherto unknown genetic evidence of a CRY-based system that is electric field sensitive in animals.

(E) Kawasaki H, Okano H, Ishiwatari H, Kishi T, Ishida N. A role of cryptochrome for magnetic field-dependent improvement of sleep quality, lifespan, and motor function in Drosophila. Genes Cells 28(7):996-522, 2023. (AS, AE, BE, DE)

Understanding the molecular genetic basis of animal magnet reception has been one of the big challenges in molecular biology. Recently it was discovered that the magnetic sense of Drosophila melanogaster is mediated by the ultraviolet (UV)-A/blue light photoreceptor cryptochrome (Cry). Here, using the fruit fly as a magnet-receptive model organism, we show that the magnetic field exposure (0.4-0.6 mT) extended lifespan under starvation, but not in cryptochrome mutant flies (cryb). The magnetic field exposure increases motor function in wild type and neurodegenerative disease model flies. Furthermore, the magnetic field exposure improved sleep quality at night-time specific manner, but not in cryb . We also showed that repeated AC magnetic field exposure increased climbing activity in wild-type Drosophila, but not in cryb . The data suggests that magnetic field-dependent improvement of lifespan, sleep quality, and motor function is mediated through a cry-dependent pathway in Drosophila.

(E) Kazemi M, H. Aliyari, S. Golabi, E. Tekieh, H. Tavakoli, M. Saberi, H. Sahraei. Improvement of Cognitive Indicators in Male Monkeys Exposed to Extremely Low-Frequency Electromagnetic Fields. Arch Razi Inst 77(1):503-511, 2022. (AS, CE, CC, MC, BE)

Today, the production of extremely low-frequency electromagnetic fields (ELF-EMFs) has significantly increased. This study aimed to investigate the effect of the ELF-EMFs on the structure and function of the brain in male rhesus monkeys in terms of visual learning (VL),

visual memory (VM), and visual working memory (VWM). To conduct the study, four monkeys were selected, of whom two monkeys were irradiated by 12-Hz ELF-EMFs with a magnitude of 0.7 microtesla, and two monkeys were tested without irradiation (control group). A blood sample was taken in three stages, namely pre- and post-irradiated and the recovery phases. Changes in the plasma levels of sodium, potassium, and adrenocorticotropic hormone (ACTH) were evaluated. Moreover, gene expression of N-methyl-D-aspartate (NMDA) receptors was assessed. The anatomical change of the brain's prefrontal area was measured by magnetic resonance imaging and Digital Imaging and Communications in Medicine LiteBox file. The abilities of VL, VM, and VWM significantly improved after the irradiation. Furthermore, the expression of the NMDA receptors gene and the plasma levels of sodium, potassium, and ACTH significantly enhanced after the irradiation. However, the prefrontal area was not significantly affected by the irradiation. No significant differences were observed in any of the studied factors in the control group. Our findings suggested that ELF-EMFs irradiation at 12 Hz positively affected VL and VWM. Consequently, 12-Hz ELF-EMFs irradiations can be widely applied to improve cognitive abilities in monkeys.

(E) Kazemi M, Sahraei H, Aliyari H, Tekieh E, Saberi M, Tavacoli H, Meftahi GH, Ghanaati H, Salehi M, Hajnasrollah M. Effects of the Extremely Low Frequency Electromagnetic Fields on NMDA-Receptor Gene Expression and Visual Working Memory in Male Rhesus Macaques. Basic Clin Neurosci. 9(3):167-176, 2018. (AS, CE, BE, CC, MA)

INTRODUCTION: The present research aimed to examine Visual Working Memory (VWM) test scores, as well as hormonal, genomic, and brain anatomic changes in the male rhesus macaques exposed to Extremely Low Frequency Magnetic Field (ELF-MF). **METHODS:** Four monkeys were exposed to two different ELF-MF frequencies: 1 Hz (control) and 12 Hz (experiment) with 0.7 μT (magnitude) 4 h/d for 30 consecutive days. Before and after the exposure, VWM test was conducted using a coated devise on a movable stand. About 10 mL of the animals' blood was obtained from their femoral vain and used to evaluate their melatonin concentration. Blood lymphocytes were used for assaying the expressions of N-Methyl-D-aspartate NMDA-receptor genes expression before and after ELF exposure. Anatomical changes of hippocampus size were also assessed using MRI images. **RESULTS:** Results indicated that VWM scores in primates exposed to 12 Hz frequency ELF increased significantly. Plasma melatonin level was also increased in these animals. However, these variables did not change in the animals exposed to 1 Hz ELF. At last, expression of the NMDA receptors increased at exposure to 12 Hz frequency. However, hippocampal volume did not increase significantly in the animals exposed to both frequencies. **CONCLUSION:** In short, these results indicate that ELF (12 Hz) may have a beneficial value for memory enhancement (indicated by the increase in VWM scores). This may be due to an increase in plasma melatonin and or expression of NMDA glutamate receptors. However, direct involvement of the hippocampus in this process needs more research.

(E)Kazemi M, Aliyari H, Tekieh E, Tavakoli H, Golabi S, Sahraei H, Meftahi GH, Sale hi M, Saberi M. The Effect of 12 Hz Extremely Low-frequency Electromagnetic Field on

Visual Memory of Male Macaque Monkeys. Basic Clin Neurosci 13(1):1-14, 2022. (AS, CE, CC, BE)

Introduction: Today, humans live in a world surrounded by electromagnetic fields. Numerous studies have been conducted to discover the biological, physiological, and behavioral effects of electromagnetic fields on humans and animals. Given the biological similarities between monkeys and humans, The present research aimed to examine Visual Memory (VM), hormonal, genomic, and anatomic changes, in the male rhesus macaques exposed to an Extremely Low-Frequency Magnetic Field (ELF-MF). **Methods:** Four male rhesus macaques (Macaca mulatta) were used. For the behavioral tests, the animals should be fasting for 17 hours. For the tests such as visual memory, the animal's cooperation was necessary. Using the radiation protocol, we exposed two monkeys to a 12-Hz electromagnetic field with a magnitude of 0.7 µT (electromagnetic radiation) four hours a day for a month. Before and after the exposure, a visual memory test was conducted using a coated device (visible reward) on a movable stand. Ten milliliters of blood was obtained from the femoral artery of each monkey, and half of it was used to examine cortisol serum levels using the MyBioSource kit (made in the USA). The other half of the blood was used to extract lymphocytes for assaying expressions of Glucocorticoid Receptor (GR) genes before and after radiation using the PCR method. Anatomic studies of the amygdala were carried out based on pre- and post-radiation Magnetic Resonance Imaging (MRI). **Results:** Research results indicated that visual memory in male primates increased significantly after exposure to the 12-Hz frequency. Hormonal analysis at the 12-Hz frequency showed a decrease in cortisol serum levels. However, visual memory and serum cortisol levels did not change considerably in male primates in the control group. There was no considerable amygdala volumetric difference after exposure to the 12-Hz frequency. The expression of the GR genes decreased in the 12-Hz group compared to the control group. **Conclusion:** In short, these results indicated that ELF might benefit memory enhancement because exposure to the 12-HZ ELF can enhance visual memory. This outcome may be due to a decrease in plasma cortisol and or expression of GR genes. Moreover, direct amygdala involvement in this regard cannot be recommended. **Highlights:** The effects of Extremely Low-Frequency Electromagnetic Fields (ELF-EMF) of 12 Hz on monkeys were studied.The results showed a reduction in the serum cortisol levels and the expression of GR genes.The amygdala anatomical area changes were not significant in the experimental group.In the experimental group, visual memory (delay of 30- and 60-s evaluation) improved after exposure to a frequency of 12 Hz. **Plain language summary:** Extremely low-frequency electromagnetic fields are among the most important factors affecting humans. This study aimed to determine the fields of 12-Hz frequency on the visual memory changes of male monkeys. The importance of research is due to the cognitive similarity of monkeys to humans. The findings of the research can be attributed to humans. Behavioral, hormonal, genetic, and anatomical studies indicated improvement in visual memory (test monkeys versus control monkeys). This study demonstrates the effect of the 12-Hz frequency on the monkey's visual memory. Researchers can study 12-Hz frequency in other cognitive indices.

(E) Kazuyoshi Kitaoka K, M Kitamura, S Aoi, N Shimizu, K Yoshizaki. Chronic exposure to an extremely low-frequency magnetic field induces depression-like behavior and corticosterone secretion without enhancement of the hypothalamic-pituitary-adrenal axis in mice. Bioelectromagnetics 34(1):43-51, 2013. (VO, LE, BE, CC)

An extremely low-frequency magnetic field (ELF-MF) is generated by power lines and household electrical devices. Many studies have suggested an association between chronic ELF-MF exposure and anxiety and/or depression. The mechanism of these effects is assumed to be a stress response induced by ELF-MF exposure. However, this mechanism remains controversial. In the present study, we investigated whether chronic ELF-MF exposure (intensity, 1.5 mT; [corrected] total exposure, 200 h) affected emotional behavior and corticosterone synthesis in mice. ELF-MF-treated mice showed a significant increase in total immobility time in a forced swim test and showed latency to enter the light box in a light-dark transition test, compared with sham-treated (control) mice. Corticosterone secretion was significantly high in the ELF-MF-exposed mice; however, no changes were observed in the amount of the adrenocorticotropic hormone and the expression of genes related to stress response. Quantification of the mRNA levels of adrenal corticosteroid synthesis enzymes revealed a significant reduction in Cyp17a1 mRNA in the ELF-MF-exposed mice. Our findings suggest the possibility that high intensity and chronic exposure to ELF-MF induces an increase in corticosterone secretion, along with depression- and/or anxiety-like behavior, without enhancement of the hypothalamic-pituitary-adrenal axis.

(E) Kesari KK, Juutilainen J, Luukkonen J, Naarala J. Induction of micronuclei and superoxide production in neuroblastoma and glioma cell lines exposed to weak 50 Hz magnetic fields. J R Soc Interface. 13(114):20150995, 2016. (CS, AE, MC, OX)

Extremely low-frequency (ELF) magnetic fields (MF) have been associated with adverse health effects in epidemiological studies. However, there is no known mechanism for biological effects of weak environmental MFs. Previous studies indicate MF effects on DNA integrity and reactive oxygen species, but such evidence is limited to MFs higher (greater than or equal to 100 μT) than those generally found in the environment. Effects of 10 and 30 μT fields were studied in SH-SY5Y and C6 cells exposed to 50-Hz MFs for 24 h. Based on earlier findings, menadione (MQ) was used as a cofactor. Responses to MF were observed in both cell lines, but the effects differed between the cell lines. Micronuclei were significantly increased in SH-SY5Y cells at 30 μT. This effect was largest at the highest MQ dose used. Increased cytosolic and mitochondrial superoxide levels were observed in C6 cells. The effects on superoxide levels were independent of MQ, enabling further mechanistic studies without co-exposure to MQ. The micronucleus and mitochondrial superoxide data were consistent with a conventional rising exposure-response relationship. For cytosolic superoxide, the effect size was unexpectedly large at 10 μT. The results indicate that the threshold for biological effects of ELF MFs is 10 μT or less. 1

(E) Keyan Z, Liqian Z, Xinzhong X, Juehua J, Chungui X. Pulsed Electromagnetic Fields Improved Peripheral Nerve Regeneration After Delayed Repair of One Month. Bioelectromagnetics 44(7-8):133-143, 2023. (AS, CE, MC, CC)

The goal of this study was to determine if postoperative pulsed electromagnetic fields (PEMFs) could improve the neuromuscular rehabilitation after delayed repair of peripheral nerve injuries.

Thirty-six Sprague-Dawley rats were randomly divided into sham group, control group, and PEMFs group. The sciatic nerves were transected except for the control group. One month later, the nerve ends of the former two groups were reconnected. PEMFs group of rats was subjected to PEMFs thereafter. Control group and sham group received no treatment. Four and 8 weeks later, morphological and functional changes were measured. Four and eight weeks postoperatively, compared to sham group, the sciatic functional indices (SFIs) of PEMFs group were higher. More axons regenerated distally in PEMFs group. The fiber diameters of PEMFs group were larger. However, the axon diameters and myelin thicknesses were not different between these two groups. The brain-derived neurotrophic factor and vascular endothelial growth factor expressions were higher in PEMFs group after 8 weeks. Semi-quantitative IOD analysis for the intensity of positive staining indicated that there were more BDNF, VEGF, and NF200 in PEMFs group. It's concluded that PEMFs have effect on the axonal regeneration after delayed nerve repair of one month. The upregulated expressions of BDNF and VEGF may play roles in this process.

(E) Kim HJ, Jung J, Park JH, Kim JH, Ko KN, Kim CW. Extremely low-frequency electromagnetic fields induce neural differentiation in bone marrow derived mesenchymal stem cells. Exp Biol Med (Maywood). 238(8):923-931, 2013. (CS, AE, MC, MA)

Extremely low-frequency electromagnetic fields (ELF-EMF) affect numerous biological functions such as gene expression, cell fate determination and even cell differentiation. To investigate the correlation between ELF-EMF exposure and differentiation, bone marrow derived mesenchymal stem cells (BM-MSCs) were subjected to a 50-Hz electromagnetic field during in vitro expansion. The influence of ELF-EMF on BM-MSCs was analysed by a range of different analytical methods to understand its role in the enhancement of neural differentiation. ELF-EMF exposure significantly decreased the rate of proliferation, which in turn caused an increase in neuronal differentiation. The ELF-EMF-treated cells showed increased levels of neuronal differentiation marker (MAP2), while early neuronal marker (Nestin) was down-regulated. In addition, eight differentially expressed proteins were detected in two-dimensional electrophoresis maps, and were identified using ESI-Q-TOF LC/MS/MS. Among them, ferritin light chain, thioredoxin-dependent peroxide reductase, and tubulin β-6 chain were up-regulated in the ELF-EMF-stimulated group. Ferritin and thioredoxin-dependent peroxide reductase are involved in a wide variety of functions, including Ca(2+) regulation, which is a critical component of neurodegeneration. We also observed that the intracellular Ca(2+) content was significantly elevated after ELF-EMF exposure, which strengthens the modulatory role of ferritin and thioredoxin-dependent peroxide reductase, during differentiation. Notably, western blot analysis indicated significantly increased expression of the ferritin light chain in the ELF-EMF-stimulated group (0.60 vs. 1.08; $P < 0.01$). These proteins may help understand the effect of ELF-EMF stimulation on BM-MSCs during neural differentiation and its potential use as a clinically therapeutic option for treating neurodegenerative diseases.

(E) Kirimoto H, Tamaki H, Otsuru N, Yamashiro K, Onishi H, Nojima I, Oliviero A. Transcranial Static Magnetic Field Stimulation over the Primary Motor Cortex

Induces Plastic Changes in Cortical Nociceptive Processing. Front Hum Neurosci. 12:63, 2018. (HU, AE, EE, MA)

Transcranial static magnetic field stimulation (tSMS) is a novel and inexpensive, non-invasive brain stimulation (NIBS) technique. Here, we performed non-invasive modulation of intra-epidermal electrical stimulation-evoked potentials (IES-EPs) by applying tSMS or sham stimulation over the primary motor (M1) and somatosensory (S1) cortices in 18 healthy volunteers for 15 min. We recorded EPs after IES before, right after, and 10 min after tSMS. The IES-EP amplitude was significantly reduced immediately after tSMS over M1, whereas tSMS over S1 and sham stimulation did not affect the IES-EP amplitude. Thus, tSMS may affect cortical nociceptive processing. Although the results of intervention for experimental acute pain in healthy subjects cannot be directly translated into the clinical situation, tSMS may be a potentially useful NIBS method for managing chronic pain, in addition to standard of care treatments.

(E) Kitaoka K, Kitamura M, Aoi S, Shimizu N, Yoshizaki K. Chronic exposure to an extremely low-frequency magnetic field induces depression-like behavior and corticosterone secretion without enhancement of the hypothalamic-pituitary-adrenal axis in mice. Bioelectromagnetics. 34(1):43-51, 2013. (AS, CE, BE, CC)

An extremely low-frequency magnetic field (ELF-MF) is generated by power lines and household electrical devices. Many studies have suggested an association between chronic ELF-MF exposure and anxiety and/or depression. The mechanism of these effects is assumed to be a stress response induced by ELF-MF exposure. However, this mechanism remains controversial. In the present study, we investigated whether chronic ELF-MF exposure (intensity, 3 mT; total exposure, 200 h) affected emotional behavior and corticosterone synthesis in mice. ELF-MF-treated mice showed a significant increase in total immobility time in a forced swim test and showed latency to enter the light box in a light-dark transition test, compared with sham-treated (control) mice. Corticosterone secretion was significantly high in the ELF-MF-exposed mice; however, no changes were observed in the amount of the adrenocorticotropic hormone and the expression of genes related to stress response. Quantification of the mRNA levels of adrenal corticosteroid synthesis enzymes revealed a significant reduction in Cyp17a1 mRNA in the ELF-MF-exposed mice. Our findings suggest the possibility that high intensity and chronic exposure to ELF-MF induces an increase in corticosterone secretion, along with depression- and/or anxiety-like behavior, without enhancement of the hypothalamic-pituitary-adrenal axis.

Klimek A., Rogalska J. Extremely Low-Frequency Magnetic Field as a Stress Factor-Really Detrimental?-Insight into Literature from the Last Decade. Brain Sci 11(2):174, 2021. (Review)

Biological effects of extremely low-frequency magnetic field (ELF-MF) and its consequences on human health have become the subject of important and recurrent public debate. ELF-MF evokes cell/organism responses that are characteristic to a general stress reaction, thus it can be regarded as a stress factor. Exposure to ELF-MF "turns on" different intracellular mechanisms into both directions: compensatory or deleterious ones. ELF-MF can provoke morphological and physiological changes in stress-related systems, mainly nervous, hormonal, and immunological

ones. This review summarizes the ELF-MF-mediated changes at various levels of the organism organization. Special attention is placed on the review of literature from the last decade. Most studies on ELF-MF effects concentrate on its negative influence, e.g., impairment of behavior towards depressive and anxiety disorders; however, in the last decade there was an increase in the number of research studies showing stimulating impact of ELF-MF on neuroplasticity and neurorehabilitation. In the face of numerous studies on the ELF-MF action, it is necessary to systematize the knowledge for a better understanding of the phenomenon, in order to reduce the risk associated with the exposure to this factor and to recognize the possibility of using it as a therapeutic agent.

(E) (AS, CE, OX) Klimek A, Nowakowska A, Kletkiewicz H, Wyszkowska J, Maliszewska J, Jankowska M, Peplowski L. Bidirectional Effect of Repeated Exposure to Extremely Low-Frequency Electromagnetic Field (50 Hz) of 1 and 7 mT on Oxidative/Antioxidative Status in Rat's Brain: The Prediction for the Vulnerability to Diseases. Oxid Med Cell Longev 2022:1031211, 2022.

Studies reported evidence for opposite effects of extremely low-frequency electromagnetic field (EMF): harmful, including the oxidative stress induction, and beneficial, such as the activation of antioxidant defense. People's exposure to EMF is often repeated or prolonged, and it is important to consider the cumulative effect of such kind of exposure on the organism. If changes evoked by repeated exposure to EMF are permanent, responsiveness to other stress factors can be modified. The aims of our study were (1) to evaluate changes in the levels of oxidative stress and antioxidant defense markers in the prefrontal cortex of adult rats after repeated exposure to 1 and 7 mT EMF and (2) to assess whether repeated EMF exposure can modify oxidative/antioxidative status in response to other stress factors. Rats were exposed to EMF 1 h/day for 7 days, one, twice, or three times. After each exposure, 8-isoprostanes, protein carbonyl groups, and the total antioxidant capacity were assessed. Part of the animals, after EMF treatment, was exposed to another stress factor-open field. Results showed that repeated exposure changed the oxidative/antioxidative status depending on the intensity of the EMF and the number of exposures. 1 mT EMF created weak changes in the oxidative status in the brain; however, 7 mT EMF moved the balance to a clearly higher level. The changes in the oxidative status after 1 mT EMF were enough to reduce, and after 7 mT EMF to intensify oxidative processes in response to the next stress. We concluded that the organism might adapt to "weak" EMF, while "strong" EMF exceeds the adaptive capacity of the organism and sensitizes it to subsequent stress, and thus may modulate vulnerability to diseases. Our results also provide new insights into the possible therapeutic properties of the magnetic field, as 1 mT EMF appears to have a potentially protective impact on the brain.

(E) Klimek A, Kletkiewicz H, Siejka A, Wyszkowska J, Maliszewska J, Klimiuk M, Milena Jankowska M, Rogalska J. The extremely low-frequency electromagnetic field (50 Hz) can establish a new "set-point" for the activity of the locus coeruleus-noradrenergic (LC-NA) system in rat. Brain Res Bull 219:111111, 2024. (AS, CE, CC, BE)

Exposure of organisms to extremely low-frequency electromagnetic field (ELF-EMF; 50 Hz) has been increasing in recent decades, which is connected with dynamic technological development. ELF-EMF is considered a stress factor and its effects on organisms are still being investigated. We aimed to determine its impact on the locus coeruleus-noradrenergic (LC-NA) system enabling adaptation to stressful conditions. For this purpose, we exposed rats to 50 Hz ELF-EMF of 1 and 7 mT, 1 h/day for 7 days. The procedure was repeated three times to examine the organism's adaptive capabilities. Subsequently, the concentration of adrenaline, noradrenaline and its metabolite MHPG as well as the expression of the β2-adrenergic receptor was assessed. After the end of each exposure, part of the animals were subjected to a behavioural test to assess the influence of repeated ELF-EMF exposure on stress response to subsequent stress factors. Our research proved that mechanisms underlying the effects of ELF-EMF on stress response include the LC-NA system. ELF-EMF of 1 mT induced adaptive changes in the NA-LC system. However, exposure to 7 mT caused increased activity of the stress system which resulted in sensitization to subsequent, heterotypic (different from the one previously acting) stress factor. As ELF-EMF of 7 mT caused a profound decrease in β2-AR level would strongly inhibit the potential for neuroplastic processes in the hippocampus. Moreover, rats exposed to ELF-EMF of 7 mT showed moderately increased anxiety-related behaviour. Disturbances in NA-LC transmission may underlie the development of some neurodegenerative and psychiatric diseases which indicates the possible involvement of ELF-EMF in the pathogenesis of these disorders.

(E) Koeman T, Schouten LJ, van den Brandt PA, Slottje P, Huss A, Peters S, Kromhout H, Vermeulen R. Occupational exposures and risk of dementia-related mortality in the prospective Netherlands Cohort Study. Am J Ind Med. 58(6):625-635, 2015. (HU, CE, ND)

BACKGROUND: Occupational exposures may be associated with non-vascular dementia. METHODS: We analyzed the effects of occupational exposures to solvents, pesticides, metals, extremely low frequency magnetic fields (ELF-MF), electrical shocks, and diesel motor exhaust on non-vascular dementia related mortality in the Netherlands Cohort Study (NLCS). Exposures were assigned using job-exposure matrices. After 17.3 years of follow-up, 682 male and 870 female cases were available. Analyses were performed using Cox regression. RESULTS: Occupational exposure to metals, chlorinated solvents and ELF-MF showed positive associations with non-vascular dementia among men, which seemed driven by metals (hazard ratio ever high vs. background exposure: 1.35 [0.98-1.86]). Pesticide exposure showed statistically significant, inverse associations with non-vascular dementia among men. We found no associations for shocks, aromatic solvents, and diesel motor exhaust. CONCLUSIONS: Consistent positive associations were found between occupational exposure to metals and non-vascular dementia. The finding on pesticides is not supported in the overall literature.

(E) Koeman T, Slottje P, Schouten LJ, Peters S, Huss A, Veldink JH, Kromhout H, van den Brandt PA, Vermeulen R. Occupational exposure and amyotrophic lateral sclerosis in a prospective cohort. Occup Environ Med. 74:578-583, 2017. (HU, ND)

OBJECTIVE: To prospectively study suspected occupational risk factors for amyotrophic lateral sclerosis (ALS). METHODS: For this case-cohort analysis within the prospective Netherlands Cohort Study, 58 279 men and 62 573 women aged 55-69 years at enrolment in 1986 were followed up for 17.3 years on ALS mortality. Information on occupational history and potential confounders were collected at

baseline through a self-administered questionnaire and entered for a random subcohort (2092 men and 2074 women) and ALS deaths (76 men and 60 women). Occupational exposure to solvents, pesticides, metals, extremely low frequency magnetic fields (ELF-MFs) and electrical shocks was estimated by means of job exposure matrices (JEMs). Associations between ever/never occupationally exposed and cumulative exposure and ALS mortality were analysed by gender using Cox regression. RESULTS: Occupational exposure to ELF-MF showed a possible association with ALS mortality among men: HR for ever holding a job with high exposure versus background 2.19 (95% (CI): 1.02 to 4.73) and HR for the highest tertile of cumulative exposure versus background 1.93 (95% CI 1.05 to 3.55). INTERPRETATION: These results strengthen the evidence suggesting a positive association between ELF-MF exposure and ALS. We did not replicate earlier positive findings for other occupational exposures.

(E) Komaki A, Khalili A, Salehi I, Shahidi S, Sarihi A. Effects of exposure to an extremely low frequency electromagnetic field on hippocampal long-term potentiation in rat. Brain Res. 1564:1-8, 2014. (AS, CE, EE)

Modern lifestyle exposes nearly all humans to electromagnetic fields, particularly extremely low frequency electromagnetic field (ELF-EMF). Prolonged exposure to ELF-EMF induces persistent changes in neuronal activity. However, the modulation of synaptic efficiency by ELF-EMF in vivo is still unclear. In the present study, we investigated whether ELF-EMF can change induction of long-term potentiation (LTP) and paired-pulse ratio (PPR) in rat hippocampal area. Twenty-nine adult male Wistar rats were divided into 3 groups (ELF-EMF exposed, sham and control groups). ELF-EMF group was exposed to the magnetic field for 90 consecutive days (2 hours/day). ELF-EMF was produced by a circular coil (50Hz, 100 micro Tesla). The sham-exposed controls were placed in an identical chamber with no electromagnetic field. After this period, rats were deeply anesthetized with urethane (2.0mg/kg) and then a bipolar stimulating and recording electrode was implanted into the perforant pathway (PP) and dentate gyrus (DG), respectively. LTP in hippocampal area was induced by high-frequency stimulation (HFS). Prolonged exposure to ELF-EMF increased LTP induction. There was a significant difference in the slope of EPSP and amplitude of PS between the ELF-EMF and other groups. In conclusion, our data suggest that exposure to ELF-EMF produces a marked change in the synaptic plasticity generated in synapses of the PP-DG. No significant difference in PPR of ELF-EMF group before and after HFS suggests a postsynaptic expression site of LTP.

(E) Korpinar MA, Kalkan MT, Tuncel H. The 50 Hz (10 mT) sinusoidal magnetic field: effects on stress-related behavior of rats. Bratisl Lek Listy. 113(9):521-524, 2012. (AS, CE, BE)

Purpose: The purpose of this study was to investigate the behavioral changes induced by 50 Hz, 10 mT flux density Sinusoidal Magnetic Field (MF). Material and methods: Seventy-six young adult male Wistar albino rats were used in the study. They were separated into two groups: control group (C) n=38; MF group n=38. C animals were left under the same conditions with the MF group for 21 days but with prevented or avoided exposure to MF. Anxiety and stress-related

behavioral changes were investigated by elevated plus-maze and hole-board systems. Just before being tested in the maze, each animal was tested by means of the hole-board method in order to separate the directed exploration behavior and locomotion activity changes from anxiety-related behavior. Results: In the hole-board system parameters there were no statistically significant differences between the two groups. There was a statistically significant difference between MF and C groups when the ratio of time spent on open arms to the total time spent on all arms was evaluated (0.12±0.08 and 0.34±0.18 respectively and $p < 0.01$). Conclusion: Our results suggest that after 21 days, a continuous exposure to extremely low frequency of magnetic field (50 Hz, 10 mT) has no significant effect on activity and exploration activity but significantly induces stress and anxiety-related behavior in rats (Tab. 2, Fig. 9, Ref. 19).

(E) Kumar A, Roy A, Karaddi V, Jain S, Katyal J, Gupta YK. Noninvasive Brain Stimulation Protects Cognitive Impairment in i.c.v. STZ-Injected Rats: Role of Adult Neurogenesis. Eur J Neurosci. 62(8):e70277, 2025. (AS, CE, MC, BE, OX, MA)

In Alzheimer's-like dementia, neurodegeneration and synaptic dysfunction are known to be the critical players in explaining cognitive impairment. Adult neurogenesis, normally a chronic and quiet process, is explained to have potential in the field of Alzheimer's therapy. Previous research on noninvasive brain stimulation showed that by controlling the pattern of stimulation externally, we can regulate/entrain neuronal activity, possibly altering the structural changes at the circuit level. However, literature investigating whether noninvasive brain stimulation could hold any potential to initiate the process of adult neurogenesis is scarce. In the present study, with the use of behavioural, microscopic and biochemical tools, we found that extremely low-frequency magnetic field at an intensity of 17.96 μT with a sinusoidal wave of 50 Hz for 2 h daily for a period of 2 weeks in a streptozotocin-induced animal model of sporadic Alzheimer's disease can cause improvement in spatial and reference memory, influencing their swimming strategy in the water maze. This is caused by stimulation in immature neural pluripotent stem cells, with additional redox balance and mitigation of glial aggravation in brain areas like the olfactory bulb, prefrontal cortex and hippocampus. These changes were accompanied by neuroprotection, as observed in the granular layer of dentate gyrus. Taken together, the present study explains a plausible mechanism of action on the protection of neurodegeneration in Alzheimer's disease through noninvasive brain stimulation.

Kumar S, Dey S, Jain S. Extremely low-frequency electromagnetic fields: A possible non-invasive therapeutic tool for spinal cord injury rehabilitation. Electromagn Biol Med. 36(1):88-101, 2017. (Review)

Traumatic insults to the spinal cord induce both immediate mechanical damage and subsequent tissue degeneration. The latter involves a range of events namely cellular disturbance, homeostatic imbalance, ionic and neurotransmitters derangement that ultimately result in loss of sensorimotor functions. The targets for improving function after spinal cord injury (SCI) are mainly directed toward limiting these secondary injury events. Extremely low-frequency

electromagnetic field (ELF-EMF) is a possible non-invasive therapeutic intervention for SCI rehabilitation which has the potential to constrain the secondary injury-induced events. In the present review, we discuss the effects of ELF-EMF on experimental and clinical SCI as well as on biological system.

(E) Kumar S, Jain S, Behari J, Avelev VD, Mathur R. Effect of magnetic field on food and water intake and body weight of spinal cord injured rats. Indian J Exp Biol. 48(10):982-986, 2010. (AS, CE, MA)

Chronic (2 h/d x 8 weeks) exposure to magnetic field (MF; 50 Hz, 17.9 microT) in complete spinal cord (T13) transected rats restored food intake (FI), water intake (WI) and body weight (BW) which were decreased in the spinal cord injured rats. The results suggest a significant beneficial effect of chronic exposure to magnetic field of paraplegic rats.

(E) Kumar S, Jain S, Velpandian T, Petrovich Gerasimenko Y, D Avelev V, Behari J, Behari M, Mathur R. Exposure to extremely low-frequency magnetic field restores spinal cord injury-induced tonic pain and its related neurotransmitter concentration in the brain. Electromagn Biol Med. 32(4):471-483, 2013. (AS, CE, BE, CC, MA)

Spinal cord injury (SCI) is unequivocally reported to produce hyperalgesia to phasic stimuli, while both hyper- and hypoalgesia to tonic stimuli. The former is spinally mediated and the latter centrally. Besides, its management is unsatisfactory. We report the effect of magnetic field (MF; 17.96 µT, 50 Hz) on tonic pain behavior and related neurotransmitters in the brain of complete thoracic (T13) SCI rats at week 8. Adult male Wistar rats were divided into Sham, SCI and SCI+MF groups. Formalin-pain behavior was compared utilizing 5 min block pain rating (PR), 60 min session-PR, time spent in various categories of increasing pain (T0-T3) and flinch incidences. Serotonin (5-HT), dopamine (DA), norepinepherine (NE), gamma-aminobutyric acid (GABA), glutamate and glycine were estimated in brain tissue by liquid chromatography-mass spectrometry. Session-PR, block-PR and number of flinches were significantly lower, while time spent in categories 0-1 was higher in the SCI versus Sham group. These parameters were comparable in the SCI+MF versus Sham group. 5-HT concentration in cortex, remaining forebrain areas and brain stem (BS), was lower while GABA and NE were higher in BS of SCI, which were comparable with Sham in the SCI+MF group. The concentration of DA, glutamate and glycine was comparable amongst the groups. The data indicate significant hypoalgesia in formalin pain while increased in GABA, NE and decreased in 5-HT post-SCI, which were restored in the SCI+MF group. We suggest beneficial effect of chronic (2 h/day × 8 weeks) exposure to MF (50 Hz, 17.96 µT) on tonic pain that is mediated by 5-HT, GABA and NE in complete SCI rats.

(E) Kumari K, Koivisto H, Viluksela M, Paldanius KMA, Marttinen M, Hiltunen M, Naarala J, Tanila H, Juutilainen J. Behavioral testing of mice exposed to intermediate frequency magnetic fields indicates mild memory impairment. PLoS One. 12(12):e0188880, 2017.(AS, CE, BE)

Human exposure to intermediate frequency magnetic fields (MF) is increasing due to applications like electronic article surveillance systems and induction heating cooking hobs.

However, limited data is available on their possible health effects. The present study assessed behavioral and histopathological consequences of exposing mice to 7.5 kHz MF at 12 or 120 µT for 5 weeks. No effects were observed on body weight, spontaneous activity, motor coordination, level of anxiety or aggression. In the Morris swim task, mice in the 120 µT group showed less steep learning curve than the other groups, but did not differ from controls in their search bias in the probe test. The passive avoidance task indicated a clear impairment of memory over 48 h in the 120 µT group. No effects on astroglial activation or neurogenesis were observed in the hippocampus. The mRNA expression of brain-derived neurotrophic factor did not change but expression of the proinflammatory cytokine tumor necrosis factor alpha mRNA was significantly increased in the 120 µT group. These findings suggest that 7.5 kHz MF exposure may lead to mild learning and memory impairment, possibly through an inflammatory reaction in the hippocampus.

(NE) Kumari K, Koivisto H, Myles C, Jonne N, Matti V, Heikki T, Jukka J. Behavioural phenotypes in mice after prenatal and early postnatal exposure to intermediate frequency magnetic fields. Environ Res. 162:27-34, 2017. (AS, CE, BE, MC)

Electromagnetic fields are ubiquitous in the environment. Human exposure to intermediate frequency (IF) fields is increasing due to applications like electronic article surveillance systems, wireless power transfer, and induction heating cooking hobs. However, there are limited data on possible health effects of exposure to IF magnetic fields (MF). In the present study, we set out to assess cognitive and behavioural effects of IF MF in mice exposed during prenatal and early postnatal periods. Pregnant female mice were exposed continuously to 7.5 kHz MFs at 12 and 120µT, from mating until weaning of pups. Sham exposed pregnant mice were used as a control group. A behavioural teratology study was conducted on the male offspring at two months of age to detect possible effects on the developing nervous system. Body weight development did not differ between the exposure groups. The exposure did not alter spontaneous motor activity when exploring a novel cage or anxiety in novelty-suppressed feeding or marble burying tests. Improved performance in the Rotarod task was observed in the 12µT group, while the 120µT exposure group swam more slowly than the sham exposed group in the Morris swim navigation task. However, indices of learning and memory (path length and escape latency during task acquisition and search bias during the probe test) did not differ between the exposure groups. Furthermore, the passive avoidance task did not indicate any impairment of long-term memory over a 48h interval in the exposed groups. In a post-mortem histopathological analysis, there was no evidence for an effect of IF MF exposure on astroglial reactivity or hippocampal neurogenesis. The results suggest that the IF MF used did not have detrimental effects on spatial learning and memory or histological markers of tissue reaction. The two statistically significant findings that were observed (improved performance in the Rotarod task in the 12µT group and decreased swimming speed in the 120µT group) are likely to be chance findings, as they do not form an internally consistent, dose-dependent pattern indicative of specific developmental effects.

(E) Lacroix A, Proulx-Bégin L, Hamel R, De Beaumont L, Bernier P-M, Lepage J-F. Static magnetic stimulation of the primary motor cortex impairs online but not offline motor sequence learning. Sci Rep 9(1):9886, 2019.(HU,AE, BE)

Static magnetic fields (SMFs) are known to alter neural activity, but evidence of their ability to modify learning-related neuroplasticity is lacking. The present study tested the hypothesis that application of static magnetic stimulation (SMS), an SMF applied transcranially via a neodymium magnet, over the primary motor cortex (M1) would alter learning of a serial reaction time task (SRTT). Thirty-nine participants took part in two experimental sessions separated by 24 h where they had to learn the SRTT with their right hand. During the first session, two groups received SMS either over contralateral (i.e., left) or ipsilateral (i.e., right) M1 while a third group received sham stimulation. SMS was not applied during the second session. Results of the first session showed that application of SMS over contralateral M1 impaired online learning as compared to both ipsilateral and sham groups, which did not differ. Results further revealed that application of SMS did not impair offline learning or relearning. Overall, these results are in line with those obtained using other neuromodulatory techniques believed to reduce cortical excitability in the context of motor learning and suggest that the ability of SMS to alter learning-related neuroplasticity is temporally circumscribed to the duration of its application.

(E) Lahijani MS, Bigdeli MR, Kalantary S. Effects of sinusoidal electromagnetic fields on histopathology and structures of brains of preincubated white Leghorn chicken embryos. Electromagn Biol Med. 30(3):146-157, 2011. (AS, AE, MC, DE)

There are several reports indicating linkages between exposures to 50-60 Hz electromagnetic fields and abnormalities in the early stages of chicken embryonic development. Based on our previous published research carried out at the Department of Animal Sciences, Faculty of Biological Sciences, Shahid Beheshti University, effects of sinusoidal electromagnetic fields on histopathology and structures of brains of preincubated white leghorn hen eggs were investigated. Three hundred healthy fresh fertilized eggs (55-65 gr) were divided into three groups of experimental (n = 50), control (n = 75), and sham (n = 75). Experimental eggs (inside the coil) were exposed to 3 different intensities of 1.33, 2.66, and 7.32 mT and sham groups were located inside the same coil with no exposure, for 24 h before incubation. Control, sham, and experimental groups were all incubated in an incubator (38 ± 0.5(°)C, 60% humidity) for 14 days. 14-day old chicken embryos were removed by C-sections, and the brains of all embryos of all groups were fixed in formalin(10%), stained with H&E and TUNEL assay, for studying the histopatholog and process of apoptosis. The brains of other embryos were prepared for Scanning Electeron Microscope. Results showed electromagnetic fields have toxic effects on brain cells by increasing the number of apoptotic cells and degeneration of brains' tissues of exposed chicken embryos. These findings suggest that the electromagnetic fields induce brain damages at different levels.

(NE) Lai J, Zhang Y, Liu X, Zhang J, Ruan G, Chaugai S, Chen C, Wang DW. Effects of extremely low frequency electromagnetic fields (100µT) on behaviors in rats. Neurotoxicology. 52:104-113, 2016. (AS, CE, BE, MC)

Recently, extremely low frequency electromagnetic fields (ELF-EMF) have received considerable attentions for their potential pathogenicity. In the present study, we explored the effects of ELF-EMF on behaviors of adult male rats. Sixty adult male rats were randomly

divided into two groups, the sham exposure group and the 50Hz/100μT ELF-EMF exposure group. During the 24 weeks exposure, body weights, as well as food and water intake were recorded. Results showed that food and water intake and the body weight of the rats were not affected by the exposure. After 24 weeks exposure, open field test and elevated plus maze were conducted to evaluate the anxiety-like behavior, the tail suspension test and forced swim test were conducted to evaluate depression-like behavior and Morris water maze and fear conditioning tests were used to evaluate the cognitive and memory ability. Exposure to ELF-EMF did not induce any anxiety-like or depression-like behaviors compared with the sham exposure. Moreover, the cognitive and memory ability was not impaired by the ELF-EMF exposure. Furthermore, ELF-EMF exposure did not affect the morphology and histology of the brain. In conclusion, 24 weeks exposure to 50Hz/100μT ELF-EMF had no effect on the behaviors of the adult male rats.

(E)Lai Y, Dong J, Wu Y, Zhao L, Wang H, Zhang J, Yao B, Xu X, Zou Y, Zhao H, Yue H, Song Y, Wang H, Peng R. Lipid Peroxides Mediated Ferroptosis in Electromagnetic Pulse-Induced Hippocampal Neuronal Damage via Inhibition of GSH/GPX4 Axis. Int J Mol Sci 23(16):9277, 2022. (AS, CS, MC, AE, BE, OX)

Electromagnetic pulse (EMP) radiation was reported to be harmful to hippocampal neurons. However, the mechanism underlying EMP-induced neuronal damage remains unclear. In this paper, for the first time, we attempted to investigate the involvement of ferroptosis in EMP-induced neuronal damage and its underlying mechanism. In vivo studies were conducted with a rat model to examine the association of ferroptosis and EMP-induced hippocampal neuronal damage. Moreover, in vitro studies were conducted with HT22 neurons to investigate the underlying mechanism of EMP-induced neuronal ferroptosis. In vivo results showed that EMP could induce learning and memory impairment of rats, ferroptotic morphological damages to mitochondria, accumulation of malonaldehyde (MDA) and iron, overexpression of prostaglandin-endoperoxide synthase 2 (PTGS2) mRNA, and downregulation of GPX4 protein in rat hippocampus. In vitro results showed that EMP could induce neuronal death, MDA accumulation, iron overload, PTGS2 overexpression, and GPX4 downregulation in HT22 neurons. These adverse effects could be reversed by either lipid peroxides scavenger ferrostatin-1 or overexpression of GPX4. These results suggest that EMP radiation can induce ferroptosis in hippocampal neurons via a vicious cycle of lipid peroxides accumulation and GSH/GPX4 axis downregulation. Lipid peroxides and the GSH/GPX4 axis provide potential effective intervention targets to EMP-induced hippocampal neuronal damage.

(E) Laszlo AM, Ladanyi M, Boda K, Csicsman J, Bari F, Serester A, Molnar Z, Sepp K, Galfi M, Radacs M. Effects of extremely low frequency electromagnetic fields on turkeys. Poult Sci. 97(2):634-642, 2018. (AS, CE, FC, CC)

Several studies have examined the potential biological effects of electromagnetic fields (EMF) on birds; however, little attention has been paid to the extremely low frequency (ELF; 0-300 Hz; 0-50 μT) radiation found in an urbanized environment. For monitoring the effects of ELF EMF, we used a turkey (Meleagris gallopavo) model, because the nucleated erythrocytes of turkeys contain β-adrenoceptors, and norepinephrine- (NE-) activated β-adrenoceptors have an important role in physiological and behavioral processes. Our aims were the following: 1) to investigate the intracellular mechanisms; 2) to compare the intracellular mechanisms in the treated and control groups over time, considering inter-individual differences and intra-subject

correlations; 3) and to study the reversible nature of the response. The turkeys in the treatment group were treated in vivo with ELF EMF (50 Hz; 10 μT) for 3 wk after a 1-wk-long adaptation period. The animals were not exposed to ELF EMF during the regeneration period (5 wk following the exposure). The NE-activated β-adrenoceptor function was detected by measuring the amount of 3´5´-cyclic-adenosine-monophosphate (cAMP), and the biochemical enzyme parameters were defined. Repeated measurements of cAMP levels were analyzed using marginal models and a piecewise linear mixed model to compare treatment and control groups over time. According to our results, NE-activated β-adrenoceptor function was decreased in the treated birds in a time-dependent manner, while there were no differences between toxicological parameters in the serum, compared to the normal ranges. The decreased NE-dependent β-adrenoceptor function could be compensated by the homeostatic complex during the 5-wk regeneration period. Extended experimental periods and more sophisticated analysis methods may help prevent harmful environmental effects on birds; furthermore, these findings could affect public health and the economy.

(E) Legros A, Corbacio M, Beuter A, Modolo J, Goulet D, Prato FS, Thomas AW. Neurophysiological and behavioral effects of a 60 Hz, 1,800 μT magnetic field in humans. Eur J Appl Physiol. 112(5):1751-1762, 2012. (HU, AE, BE)

The effects of time-varying magnetic fields (MF) on humans have been actively investigated for the past three decades. One important unanswered question is the potential for MF exposure to have acute effects on human biology. Different strategies have been used to tackle this question using various physiological, neurophysiological and behavioral indicators. For example, researchers investigating electroencephalography (EEG) have reported that extremely low frequency (ELF, <300 Hz) MF can increase resting occipital alpha rhythm (8-12 Hz). Interestingly, other studies have demonstrated that human motricity can be modulated by ELF MF: a reduction of anteroposterior standing balance or a decrease of physiological tremor intensity have been reported as consequences of exposure. However, the main limitation in this domain lies in the lack of results replication, possibly originating from the large variety of experimental approaches employed. Therefore, the present study aimed to investigate the effects of a 60 Hz, 1,800 μT MF exposure on neurophysiological (EEG) and neuromotor (standing balance, voluntary motor function, and physiological tremor) aspects in humans using a single experimental procedure. Though results from this study suggest a reduction of human standing balance with MF exposure, as well as an increase of physiological tremor amplitude within the frequency range associated with central nervous system contribution, no exposure effect appeared on other investigated parameters (e.g., EEG or voluntary motor control). These results suggest that 1 h of 60 Hz, 1,800 μT MF exposure may modulate human involuntary motor control without being detected in the cortical electrical activity.

(E) Legros A, Modolo J, Brown S, Roberston J, Thomas AW. Effects of a 60 Hz Magnetic Field Exposure Up to 3000 μT on Human Brain Activation as Measured by Functional Magnetic Resonance Imaging. PLoS One. 10(7):e0132024, 2015. (HU, AE, BE, FC)

Several aspects of the human nervous system and associated motor and cognitive processes have been reported to be modulated by extremely low-frequency (ELF, < 300 Hz) time-varying Magnetic Fields (MF). Due do their worldwide prevalence; power-line frequencies (60 Hz in North America) are of particular interest. Despite intense research efforts over the last few

decades, the potential effects of 60 Hz MF still need to be elucidated, and the underlying mechanisms to be understood. In this study, we have used functional Magnetic Resonance Imaging (fMRI) to characterize potential changes in functional brain activation following human exposure to a 60 Hz MF through motor and cognitive tasks. First, pilot results acquired in a first set of subjects (N=9) were used to demonstrate the technical feasibility of using fMRI to detect subtle changes in functional brain activation with 60 Hz MF exposure at 1800 μT. Second, a full study involving a larger cohort of subjects tested brain activation during 1) a finger tapping task (N=20), and 2) a mental rotation task (N=21); before and after a one-hour, 60 Hz, 3000 μT MF exposure. The results indicate significant changes in task-induced functional brain activation as a consequence of MF exposure. However, no impact on task performance was found. These results illustrate the potential of using fMRI to identify MF-induced changes in functional brain activation, suggesting that a one-hour 60 Hz, 3000 μT MF exposure can modulate activity in specific brain regions after the end of the exposure period (i.e., residual effects). We discuss the possibility that MF exposure at 60 Hz, 3000 μT may be capable of modulating cortical excitability via a modulation of synaptic plasticity processes.

(E) Leone L, Fusco S, Mastrodonato A, Piacentini R, Barbati SA, Zaffina S, Pani G, Podda MV, Grassi C. Epigenetic Modulation of Adult Hippocampal Neurogenesis by Extremely Low-Frequency Electromagnetic Fields. Mol Neurobiol. 49:1472-1486, 2014. (AS, CS, CE, AE, BE, CC, MA)

Throughout life, adult neurogenesis generates new neurons in the dentate gyrus of hippocampus that have a critical role in memory formation. Strategies able to stimulate this endogenous process have raised considerable interest because of their potential use to treat neurological disorders entailing cognitive impairment. We previously reported that mice exposed to extremely low-frequency electromagnetic fields (ELFEFs) showed increased hippocampal neurogenesis. Here, we demonstrate that the ELFEF-dependent enhancement of hippocampal neurogenesis improves spatial learning and memory. To gain insights on the molecular mechanisms underlying ELFEFs' effects, we extended our studies to an in vitro model of neural stem cells (NSCs) isolated from the hippocampi of newborn mice. We found that ELFEFs enhanced proliferation and neuronal differentiation of hippocampal NSCs by regulation of epigenetic mechanisms leading to pro-neuronal gene expression. Upon ELFEF stimulation of NSCs, we observed a significant enhancement of expression of the pro-proliferative gene hairy enhancer of split 1 and the neuronal determination genes NeuroD1 and Neurogenin1. These events were preceded by increased acetylation of H3K9 and binding of the phosphorylated transcription factor cAMP response element-binding protein (CREB) on the regulatory sequence of these genes. Such ELFEF-dependent epigenetic modifications were prevented by the Ca_v1-channel blocker nifedipine, and were associated with increased occupancy of CREB-binding protein (CBP) to the same loci within the analyzed promoters. Our results unravel the molecular mechanisms underlying the ELFEFs' ability to improve endogenous neurogenesis, pointing to histone acetylation-related chromatin remodeling as a critical determinant. These findings could pave the way to the development of novel therapeutic approaches in regenerative medicine.

(E) Li C, Xie M, Luo F, He C, Wang J, Tan G, Hu Z. The extremely low-frequency magnetic field exposure differently affects the AMPAR and NMDAR subunit expressions in the hippocampus, entorhinal cortex and prefrontal cortex without effects on the rat spatial learning and memory. Environ Res. 2014 134C:74-80, 2014. (AS; CE; CC)

In the present study, we investigated the effects of chronic exposure (14 and 28 days) to a 50Hz, 0.5mT extremely low-frequency magnetic field (ELF-MF) on the NMDAR and AMPAR subunit expressions and rat spatial learning and memory. Using the Western blotting method, we found ELF-MF exposure specifically decreased the expressions of GluA2 in the EC post 28 day exposure and GluA3 of AMPAR subunits in the PFC after 14 day exposure, while it did not affect the AMPAR subunit expression in the hippocampus at both time points. As for NMDAR subunits, 14 day ELF-MF exposure significantly increased the levels of GluN2A and GluN2B in the hippocampus. Moreover, the levels of GluN1 and GluN2A were enhanced in the EC and PFC after two weeks of ELF-MF exposure. Interestingly, 28 day ELF-MF exposure induced a different expression pattern for NMDAR subunits. The increased GluN2A expression observed at 14 day post ELF-MF exposure was recovered after prolonged exposure in the hippocampus and PFC. In the EC, the increased expression of GluN1 achieved to control level and, specifically, a decrease in GluN2A level was observed. Surprisingly, neither 14 nor 28 day ELF-MF did affect the rat spatial reference memory as assessed by water maze. <u>These results indicate that the dynamic and brain-region specific changes in ionotropic glutamate receptor expression induced by ELF-MF are insufficient to influence the rat spatial learning ability.</u>

(NE) Li L, Xiong DF, Liu JW, Li ZX, Zeng GC, Li HL. No effects of power line frequency extremely low frequency electromagnetic field exposure on selected neurobehavior tests of workers inspecting transformers and distribution line stations versus controls. Australas Phys Eng Sci Med. 37(1):37-44, 2014. (HU, BE, CE)

We aimed to evaluate the interference of 50 Hz extremely low frequency electromagnetic field (ELF-EMF) occupational exposure on the neurobehavior tests of workers performing tour-inspection close to transformers and distribution power lines. Occupational short-term "spot" measurements were carried out. 310 inspection workers and 300 logistics staff were selected as exposure and control. The neurobehavior tests were performed through computer-based neurobehavior evaluation system, including mental arithmetic, curve coincide, simple visual reaction time, visual retention, auditory digit span and pursuit aiming. In 500 kV areas electric field intensity at 71.98 % of total measured 590 spots were above 5 kV/m (national occupational standard), while in 220 kV areas electric field intensity at 15.69 % of total 701 spots were above 5 kV/m. Magnetic field flux density at all the spots was below 1,000 µT (ICNIRP occupational standard). The neurobehavior score changes showed no statistical significance. Results of neurobehavior tests among different age, seniority groups showed no significant changes. <u>Neurobehavior changes caused by daily repeated ELF-EMF exposure were not observed in the current study.</u>

(E) Li X, Xu H, Lei T, Yang Y, Jing D, Dai S, Luo P, Xu Q. A Pulsed Electromagnetic Field Protects against Glutamate-Induced Excitotoxicity by Modulating the Endocannabinoid System in HT22 Cells. Front Neurosci. 11:42, 2017. (CS, AE, CC, MC, ND, MA)

Glutamate-induced excitotoxicity is common in the pathogenesis of many neurological diseases. A pulsed electromagnetic field (PEMF) exerts therapeutic effects on the nervous system, but its specific mechanism associated with excitotoxicity is still unknown. We investigated the role of PEMF exposure in regulating glutamate-induced excitotoxicity through the endocannabinoid (eCB) system. PEMF exposure improved viability of HT22 cells after excitotoxicity and reduced lactate dehydrogenase release and cell death. An eCB receptor 1 (CB1R) specific inhibitor suppressed the protective effects of PEMF exposure, even though changes in CB1R expression were not observed. Elevation of N-arachidonylethanolamide (AEA) and 2-arachidonylglycerol (2-AG) following PEMF exposure indicated that the neuroprotective effects of PEMF were related to modulation of the eCB metabolic system. Furthermore, CB1R/ERK signaling was shown to be an important downstream pathway of PEMF in regulating excitotoxicity. These results suggest that PEMF exposure leads to neuroprotective effects against excitotoxicity by facilitating the eCB/CB1R/ERK signaling pathway. Therefore, PEMF may be a potential physical therapeutic technique for preventing and treating neurological diseases.

(E) Li Y, Yan X, Liu J, Li L, Hu X, Sun H, Tian J. Pulsed electromagnetic field enhances brain-derived neurotrophic factor expression through L-type voltage-gated calcium channel- and Erk-dependent signaling pathways in neonatal rat dorsal root ganglion neurons. Neurochem Int. 75:96-104, 2014a. (CS, AE, CC)

Although pulsed electromagnetic field (PEMF) exposure has been reported to promote neuronal differentiation, the mechanism is still unclear. Here, we aimed to examine the effects of PEMF exposure on brain-derived neurotrophic factor (Bdnf) mRNA expression and the correlation between the intracellular free calcium concentration ([Ca(2+)]i) and Bdnf mRNA expression in cultured dorsal root ganglion neurons (DRGNs). Exposure to 50Hz and 1mT PEMF for 2h increased the level of [Ca(2+)]i and Bdnf mRNA expression, which was found to be mediated by increased [Ca(2+)]i from Ca(2+) influx through L-type voltage-gated calcium channels (VGCCs). However, calcium mobilization was not involved in the increased [Ca(2+)]i and BDNF expression, indicating that calcium influx was one of the key factors responding to PEMF exposure. Moreover, PD098059, an extracellular signal-regulated kinase (Erk) inhibitor, strongly inhibited PEMF-dependant Erk1/2 activation and BDNF expression, indicating that Erk activation is required for PEMF-induced upregulation of BDNF expression. These findings indicated that PEMF exposure increased BDNF expression in DRGNs by activating Ca(2+)- and Erk-dependent signaling pathways.

(NE) Li Y, Zhang C, Song T. Disturbance of the magnetic field did not affect spatial memory. Physiol Res. 46: 377-385, 2014b (AS, CE, BE)

Extremely low-frequency magnetic field (ELF-MF) has been suggested to influence the cognitive capability and has to be dynamically evaluated in a longitudinal study. Previous training can affect performance, but the influence under magnetic field is unclear. This study aims to

evaluate the effects of previous training and ELF-MF exposure on learning and memory using the Morris water maze (MWM). Sprague-Dawley rats were subjected to MWM training, ELF-MF exposure (50 Hz, 100 microT), or ELF-MF exposure combined with MWM training for 90 days. Normal rats were used as controls. The MWM was used to test. The data show that the rats exposed to training and ELF-MF with training performed better on spatial acquisition when re-tested. However, during the probe trial the rats showed no change between the training phase and the test phase. Compared with the control group, the ELF-MF group showed no significant differences. These results confirm that previous training can improve the learning and memory capabilities regarding spatial acquisition in the MWM and this effect can last for at least 90 days. However, this improvement in learning and memory capabilities was not observed during the probe trial. Furthermore, ELF-MF exposure did not interfere with the improvement in learning and memory capabilities.

(E) Li Y, Zhang Y, Wang W, Zhang Y, Yu Y, Cheing GL, Pan W. Effects of pulsed electromagnetic fields on learning and memory abilities of STZ-induced dementia rats. Electromagn Biol Med. 38:123-130, 2019. (AS, CE, BE, ND, MA)

INTRODUCTION: Recent studies have shown that pulsed electromagnetic field (EMF) has therapeutic potential for dementia, but the associated neurobiological effects are unclear. This study aimed to determine the effects of pulsed EMF on Streptozotocin (STZ)-induced dementia rats. METHODS: Forty Sprague-Dawley rats were randomly allocated to one of the four groups: (i) control, (ii) normal saline injection (sham group), (iii) STZ injection (STZ group) and (iv) STZ injection with pulsed EMF exposure (PEMF, 10 mT at 20 Hz) (STZ + MF group). Morris water maze was used to assess the learning and memory abilities. Insulin growth factors 1 and 2 (IGF-1 and IGF-2) gene expression were determined by quantitative PCR. RESULTS: The results showed that the mean escape latency in STZ-induced dementia rats was reduced by 66% under the exposure of pulsed EMF. Compared with the STZ group, the swimming distance and the time for first crossing the platform decreased by 55 and 41.6% in STZ + MF group, respectively. Furthermore, the IGF-2 gene expression significantly increased compared to that of the STZ group. CONCLUSIONS: Our findings indicate that the pulsed EMF exposure can improve the ability of learning and memory in STZ-induced dementia rats and this effect may be related to the process of IGF signal transduction, suggesting a potential role for the pulsed EMF for the amelioration of cognition impairment.

(E) Liang P, Li Z, Li J, Wei J, Li J, Zhang S, Xu S, Liu Z, Wang J. Impacts of complex electromagnetic radiation and low-frequency noise exposure conditions on the cognitive function of operators. Front Public Health 11:1138118, 2023. (AE, HU, BE, IA)

Background: Both electromagnetic radiation (EMR) and low-frequency noise (LFN) are widespread and influential environmental factors, and operators are inevitably exposed to both EMR and LFN within a complex exposure environment. The potential adverse effects of such exposure on human health must be considered seriously. This study aimed to investigate the effects of EMR and LFN on cognitive function as well as their interaction effect, which remain unclear. **Methods:** Sixty young male college students were randomly grouped and experiments

were conducted with a 2 × 2 factorial design in a shielded chamber. Mental workload (MWL) levels of the study subjects were measured and assessed using the NASA-task load index (TLX) subjective scale, an n-back task paradigm, and the functional near-infrared spectroscopy (fNIRS) imaging technique. **Results:** For the 3-back task, the NASA-TLX subjective scale revealed a statistically significant main effect of LFN intensity, which enhanced the subjects' MWL level ($F = 8.716$, $p < 0.01$). Behavioral performance revealed that EMR intensity (430.1357 MHz, 10.75 W/m2) and LFN intensity (0-200 Hz, 72.9 dB) had a synergistic interaction effect, and the correct response time was statistically significantly prolonged by the combined exposure ($F = 4.343$, $p < 0.05$). The fNIRS imaging technique revealed a synergistic interaction effect between operational EMR intensity and operational LFN intensity, with statistically significant effects on the activation levels in the left and right dorsolateral prefrontal cortex (DLPFC). The mean β values of DLPFC were significantly increased (L-DLPFC $F = 5.391$, $p < 0.05$, R-DLPFC $F = 4.222$, $p < 0.05$), and the relative concentrations of oxyhemoglobin in the DLPFC were also significantly increased (L-DLPFC $F = 4.925$, $p < 0.05$, R-DLPFC $F = 9.715$, $p < 0.01$). **Conclusion:** We found a statistically significant interaction effect between EMR (430.1357 MHz, 10.75 W/m2) and LFN (0-200 Hz, 72.9 dB) when simultaneously exposing subjects to both for 30 min. We conclude that exposure to this complex environment can cause a statistically significant increase in the MWL level of operators, and even alterations in their cognitive function.

Liboff AR. The electromagnetic basis of social interactions. Electromagn Biol Med. 36(2):177-181, 2017. (opinion)

It has been established that living things are sensitive to extremely low-frequency magnetic fields at vanishingly small intensities, on the order of tens of nT. We hypothesize, as a consequence of this sensitivity, that some fraction of an individual's central nervous system activity can be magnetically detected by nearby individuals. Even if we restrict the information content of such processes to merely simple magnetic cues that are unconsciously received by individuals undergoing close-knit continuing exposure to these cues, it is likely that they will tend to associate these cues with the transmitting individual, no less than would occur if such signals were visual or auditory. Furthermore, following what happens when one experiences prolonged exposure to visual and like sensory inputs, it can be anticipated that such association occurring magnetically will eventually also enable the receiving individual to bond to the transmitting individual. One can readily extrapolate from single individuals to groups, finding reasonable explanations for group behavior in a number of social situations, including those occurring in families, animal packs, gatherings as found in concerts, movie theaters and sports arenas, riots and selected predatory/prey situations. The argument developed here not only is consistent with the notion of a magnetic sense in humans, but also provides a new approach to electromagnetic hypersensitivity, suggesting that it may simply result from sensory overload.

Liboff AR. Magnetic correlates in electromagnetic consciousness. Electromagn Biol Med. 35(3):228-236, 2016. (opinion)

We examine the hypothesis that consciousness is a manifestation of the electromagnetic field, finding supportive factors not previously considered. It is not likely that traditional electrophysiological signaling modes can be readily transmitted throughout the brain to properly enable this field because of electric field screening arising from the ubiquitous distribution of high dielectric lipid membranes, a problem that vanishes for low-frequency magnetic fields. Many reports over the last few decades have provided evidence that living tissue is robustly sensitive to ultrasmall (1-100 nT) ELF magnetic fields overlapping the γ-frequency range often associated with awareness. An example taken from animal behavior (coherent bird flocking) lends support to the possibility of a disembodied electromagnetic consciousness. In contrast to quantum consciousness hypotheses, the present approach is open to experimental trial.

Liboff AR. Is the geomagnetic map imprinted in pre-emergent egg? Electromagn Biol Med. 35(2):167-169, 2016. (opinion)

Although it is well-accepted that the geomagnetic field (GMF) plays an important role in animal navigation and migration, key problems remain unanswered. To explain the puzzling ability of hatchlings to embark on unexplored migrational journeys we hypothesize that mothers who have previously navigated the trip enable their offspring by direct transfer of route information to their eggs prior to hatching. The freshly hatched animal registers the local GMF as a reference point before embarking on the journey the mother has prepared for it. This process represents a novel type of biological cycle that finesses the need to treat questions such as natal homing and route parameters separately.

(NE) Liimatainen A, Roivainen P, Juutilainen J, Höytö A, Naarala J. A Cohort Study on Alzheimer's Disease in Relation to Residential Magnetic Fields From Indoor Transformer Stations. Bioelectromagnetics. 46(8):e70031, 2025. (HU, CE, ND)

Meta-analyses of epidemiological studies have suggested that Alzheimer's disease (AD) may be linked with exposure to extremely low frequency (ELF) magnetic fields (MF). This is the first study investigating the association of AD with exposure to residential ELF MFs from indoor transformer stations, using a study design that avoids shortcomings of previous studies. All cohort members had lived in buildings with indoor transformer stations. MF exposure was assessed based on the location of their apartment in relation to the transformer room. AD patients were identified from Drug Purchase Register and Drug Reimbursement Register. Out of the 155,562 individuals, 5652 (111,357 person-years of follow-up) living in apartments next to transformer stations were considered as exposed, while 115,772 (2,289,526 person-years of follow-up) individuals living on higher floors of the same buildings were considered as referents. Associations between MF exposure and AD were examined using Cox proportional hazard models. The hazard ratio (HR) was 1.02 (95% confidence interval: 0.85-1.22), indicating that the risk of AD is not associated with residential ELF MFs present in apartments next to transformer stations. The duration of residence did not essentially change the HR. The risk of AD was

slightly but not statistically significantly higher (HR 1.22, 95% confidence interval: 0.94-1.57) for those whose residence started before the age of 50 years. The results did not support positive findings from previous studies that have reported a link between AD and occupational or residential MF exposure.

(E) Lin Y, Lang H, Gao P, Miao X, Guo Q, Hao Y, Ai T, Li J, Zhang J, Guo G. Electromagnetic pulse exposure induces neuroinflammation and blood-brain barrier disruption by activating the NLRP3 inflammasome/NF-κB signaling pathway in mice. Ecotoxicol Environ Saf 292:117972, 2025. (AS, CE, CC, OX, MC)

The electromagnetic pulse (EMP) is a widespread electromagnetic disturbance that can disrupt electronic systems and pose health risks to personnel in operational areas. The biological effects of EMP radiation, especially on the central nervous system (CNS), are not yet fully understood but are gaining attention. This study examines the impact of EMP on the CNS using microglial cells as a model system. We found that mice exposed to a field strength of 600 kV/m with 1000 pulses per day for two weeks exhibited increased levels of oxidative stress. This exposure induced a microglia polarization to the M1 state, leading to neuroinflammation and disruption of the blood-brain barrier (BBB) by the pro-inflammatory response of microglia. Further analysis revealed that the NLRP3 inflammasome/NF-κB signaling pathway modulates the pro-inflammatory mechanisms of EMP irradiation. In conclusion, our findings show that EMP irradiation triggers neuroinflammation and BBB damage via NLRP3 inflammasome/NF-κB activation. This research highlights the effects of EMP radiation on the CNS and offers valuable insights into the potential targets for biomedical protection against it.

(E) Liu DD, Ren Z, Yang G, Zhao QR, Mei YA. Melatonin protects rat cerebellar granule cells against electromagnetic field-induced increases in Na+ currents through intracellular Ca2+ release. J Cell Mol Med. 18(6):1060-1070, 2014. (CS, AE, CC, OX)

Although melatonin (MT) has been reported to protect cells against oxidative damage induced by electromagnetic radiation, few reports have addressed whether there are other protective mechanisms. Here, we investigated the effects of MT on extremely low-frequency electromagnetic field (ELF-EMF)-induced Na_v activity in rat cerebellar granule cells (GCs). Exposing cerebellar GCs to ELF-EMF for 60 min. significantly increased the Na_v current (I_{Na}) densities by 62.5%. MT (5 µM) inhibited the ELF-EMF-induced I_{Na} increase. This inhibitory effect of MT is mimicked by an MT_2 receptor agonist and was eliminated by an MT_2 receptor antagonist. The Na_v channel steady-state activation curve was significantly shifted towards hyperpolarization by ELF-EMF stimulation but remained unchanged by MT in cerebellar GC that were either exposed or not exposed to ELF-EMF. ELF-EMF exposure significantly increased the intracellular levels of phosphorylated PKA in cerebellar GCs, and both MT and IIK-7 did not reduce the ELF-EMF-induced increase in phosphorylated PKA. The inhibitory effects of MT on ELF-EMF-induced Na_v activity was greatly reduced by the calmodulin inhibitor KN93. Calcium imaging showed that MT did not increase the basal intracellular Ca^{2+} level, but it significantly elevated the intracellular Ca^{2+} level evoked by the high K^+ stimulation in cerebellar GC that were

either exposed or not exposed to ELF-EMF. In the presence of ruthenium red, a ryanodine-sensitive receptor blocker, the MT-induced increase in intracellular calcium levels was reduced. Our data show for the first time that MT protects against neuronal I_{Na} that result from ELF-EMF exposure through Ca^{2+} influx-induced Ca^{2+} release.

(E) Liu H, Chen G, Pan Y, Chen Z, Jin W, Sun C, Chen C, Dong X, Chen K, Xu Z, Zhang S, Yu Y. Occupational Electromagnetic Field Exposures Associated with Sleep Quality: A Cross-Sectional Study. PLoS ONE 9(10): e110825, 2014. (HU, CE, BE)

BACKGROUND: Exposure to electromagnetic field (EMF) emitted by mobile phone and other machineries concerns half the world's population and raises the problem of their impact on human health. The present study aims to explore the effects of electromagnetic field exposures on sleep quality and sleep duration among workers from electric power plant. METHODS: A cross-sectional study was conducted in an electric power plant of Zhejiang Province, China. A total of 854 participants were included in the final analysis. The detailed information of participants was obtained by trained investigators using a structured questionnaire, which including socio-demographic characteristics, lifestyle variables, sleep variables and electromagnetic exposures. Physical examination and venous blood collection were also carried out for every study subject. RESULTS: After grouping daily occupational electromagnetic exposure into three categories, subjects with long daily exposure time had a significantly higher risk of poor sleep quality in comparison to those with short daily exposure time. The adjusted odds ratios were 1.68 (95%CI: 1.18, 2.39) and 1.57 (95%CI: 1.10, 2.24) across tertiles. Additionally, among the subjects with long-term occupational exposure, the longer daily occupational time apparently increased the risk of poor sleep quality (OR (95%CI): 2.12 (1.23~3.66) in the second tertile; 1.83 (1.07~3.15) in the third tertile). There was no significant association of long-term occupational exposure duration, monthly electric fee or years of mobile-phone use with sleep quality or sleep duration. CONCLUSIONS: The findings showed that daily occupational EMF exposure was positively associated with poor sleep quality. It implies EMF exposure may damage human sleep quality rather than sleep duration.

(E) Liu T, Wang S, He L, Ye K. Anxiogenic effect of chronic exposure to extremely low frequency magnetic field in adult rats. Neurosci Lett. 434(1):12-17, 2008a. (AS, CE, BE)

Previous study has suggested some relations between extremely low frequency magnetic field (ELF MF) and the emotional state of human beings and animals. The aim of the present study was to investigate whether the anxiety level could be affected by repeated ELF MF exposure of different daily durations. Adult SD rats were submitted to no exposure, MF exposure 1h/day or 4h/day for 25 days. Anxiety-related behaviors were examined in the open field test (OFT), the elevated plus maze (EPM), and light/dark box on the 21th, 23th and 25th exposure day, respectively. Results demonstrated that MF exposure 4h/day increased the anxiety-like behaviors in rats in the open field test and the elevated plus maze test, without altering their locomotor activity, but had no effect in the light/dark box test. Moreover, MF exposure 1h/day had no effect in any test. These findings indicate that chronic ELF MF exposure has anxiogenic

effect in rats, which is dependent on the daily exposure duration and it is more sensitive to void space than to strong light.

(E) Liu T, Wang S, He L, Ye K. Chronic exposure to low-intensity magnetic field improves acquisition and maintenance of memory. Neuroreport. 19(5):549-552, 2008b. (AS, CE, BE)

Although past research has suggested that acute exposure to extremely low-frequency magnetic field (ELF MF) impairs learning and memory function, data on chronic exposure remain scarce. In this study, we examined the changes in spatial learning and memory by the Morris water maze test after 4 weeks of daily exposure of rats to a 50-Hz magnetic field of 2 mT for either 1 or 4 h. We found that chronic exposure to ELF MF reduced the latency to find the hidden platform and improved long-term memory of former location of platform without affecting the short-term memory and motor activity. These findings for the first time indicate that chronic exposure to ELF MF exerts a positive effect on the acquisition and maintenance of spatial memory.

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(E) Liu X, Zuo H, Wang D, Peng R, Song T, Wang S, Xu X, Gao Y, Li Y, Wang S, Wang L, Zhao L. Improvement of spatial memory disorder and hippocampal damage by exposure to electromagnetic fields in an Alzheimer's disease rat model. PLoS One. 10(5):e0126963, 2015. (AS, CE, BE, FC, OX, MA)

Although some epidemiological investigations showed a potential association between long-term exposure of extremely low frequency electromagnetic fields (ELF-EMF) and Alzheimer's disease (AD), no reasonable mechanism can explain this association, and the related animal experiments are rare. In this study, ELF-EMF exposure (50 Hz 400 μT 60 d) combined with D-galactose intraperitoneal (50 mg/kg, q.d., 42 d) and Aβ25-35 hippocampal (5 μl/unilateral, bilateral, single-dose) injection was implemented to establish a complex rat model. Then the effects of ELF-EMF exposure on AD development was studied by using the Morris water maze, pathological analysis, and comparative proteomics. The results showed that ELF-EMF exposure delayed the weight gain of rats, and partially improved cognitive and clinicopathologic symptoms of AD rats. The differential proteomic analysis results suggest that synaptic transmission, oxidative stress, protein degradation, energy metabolism, Tau aggregation, and inflammation involved in the effects mentioned above. Therefore, our findings indicate that certain conditions of ELF-EMF exposure could delay the development of AD in rats.

(E) Lobyntseva A, Ganaiem M, Ivashko-Pachima Y, Barnstable CJ, Weisinger B, Parabucki A, Segal Y, Shohami E, Gozes I. Extremely Low-Frequency and Low-Intensity Electromagnetic Field Technology (ELF-EMF) Sculpts Microtubules. Eur J Neurosci 61(4):e70023, 2025. (CS, AE, CC, MA, ND)

Aberrant microtubule dynamics coupled with a reduction in Tau-microtubule interaction are at the core of neuronal injuries resulting in microtubule disruption and aggregates of abnormally phosphorylated Tau. These pathological Tau aggregates define tauopathies such as Alzheimer's disease (AD), as well as the pathological sequelae following traumatic brain injury (TBI), stroke

and spinal cord injury (SCI). We hypothesized that differential applications of extremely low-frequency and low-intensity electromagnetic field (ELF-EMF) will change microtubule function. To examine our hypothesis, we pre-applied ELF-EMF to a neuroblastoma neuronal cell line later exposed to 4 h of zinc intoxication, modelling Tau-microtubule dissociation. ELF-EMF (40 Hz and 1 G; multiple exposure schedules) enhanced microtubule dynamics and increased Tau-microtubule interaction in the face of zinc toxicity. Complementing these preconditioning neuroprotective effects, concomitant 1 h treatment protocols comparing 3.9 or 40 Hz and 1 G exposure, indicated effects on Tau phosphorylation accentuated with 40 Hz and reduction in beta tubulin isotypes, depending on electromagnetic frequencies, most pronounced at 3.9 Hz. Our results discovered ELF-EMF modulation on the microtubule cytoskeleton essential for brain health.

(E) Lozano-Soto E, Soto-León V, Sabbarese S, Ruiz-Alvarez L, Sanchez-Del-Rio M, Aguilar J, Strange BA, Foffani G, Oliviero A. Transcranial static magnetic field stimulation (tSMS) of the visual cortex decreases experimental photophobia. Cephalalgia. 38(8):1493-1497, 2018. (HU, AE, BE, MA)

Background Transcranial static magnetic field stimulation (tSMS) reduces cortical excitability in humans. Methods The objective of this study was to determine whether tSMS over the occipital cortex is effective in reducing experimental photophobia. In a sham-controlled double-blind crossover study, tSMS (or sham) was applied for 10 minutes with a cylindrical magnet on the occiput of 20 healthy subjects. We assessed subjective discomfort induced by low-intensity and high-intensity visual stimuli presented in a dark room before, during and after tSMS (or sham). Results Compared to sham, tSMS significantly reduced the discomfort induced by high-intensity light stimuli. Conclusions The visual cortex may contribute to visual discomfort in experimental photophobia, providing a rationale for investigating tSMS as a possible treatment for photophobia in migraine.

(E) Lundberg L, Sienkiewicz Z, Anthony DC, Broom KA. Effects of 50 Hz magnetic fields on circadian rhythm control in mice. Bioelectromagnetics. 40(4):250-259, 2019. (AS, AE, BE)

Artificial light and power frequency magnetic fields are ubiquitous in the built environment. Light is a potent zeitgeber but it is unclear whether power frequency magnetic fields can influence circadian rhythm control. To study this possibility, 8-12-week-old male C57BL/6J mice were exposed for 30 min starting at zeitgeber time 14 (ZT14, 2 h into the dark period of the day) to 50 Hz magnetic fields at 580 μT using a pair of Helmholtz coils and/or a blue LED light at 700 lux or neither. Our experiments revealed an acute adrenal response to blue light, in terms of increased adrenal per1 gene expression, increased serum corticosterone levels, increased time spent sleeping, and decreased locomotor activity (in all cases, $P < 0.0001$) compared to an unexposed control group. There appeared to be no modulating effect of the magnetic fields on the response to light, and there was also no effect of the magnetic fields alone (in both cases, $P > 0.05$) except for a decrease in locomotor activity ($P < 0.03$). Gene expression

of the cryptochromes cry1 and cry2 in the adrenals, liver, and hippocampus was also not affected by exposures (in all cases, P > 0.05). In conclusion, these results suggest that 50 Hz magnetic fields do not significantly affect the acute light response to a degree that can be detected in the adrenal response.

(E) Ma Q, Chen C, Deng P, Zhu G, Lin M, Zhang L, Xu S, He M, Lu Y, Duan W, Pi H, Cao Z, Pei L, Li M, Liu C, Zhang Y, Zhong M, Zhou Z, Yu Z. Extremely Low-Frequency Electromagnetic Fields Promote In Vitro Neuronal Differentiation and Neurite Outgrowth of Embryonic Neural Stem Cells via Up-Regulating TRPC1. PLoS One. 11(3):e0150923, 2016. (AS, CE, MC, DE)

Exposure to extremely low-frequency electromagnetic fields (ELF-EMFs) can enhance hippocampal neurogenesis in adult mice. However, little is focused on the effects of ELF-EMFs on embryonic neurogenesis. Here, we studied the potential effects of ELF-EMFs on embryonic neural stem cells (eNSCs). We exposed eNSCs to ELF-EMF (50 Hz, 1 mT) for 1, 2, and 3 days with 4 hours per day. We found that eNSC proliferation and maintenance were significantly enhanced after ELF-EMF exposure in proliferation medium. ELF-EMF exposure increased the ratio of differentiated neurons and promoted the neurite outgrowth of eNSC-derived neurons without influencing astrocyes differentiation and the cell apoptosis. In addition, the expression of the proneural genes, NeuroD and Ngn1, which are crucial for neuronal differentiation and neurite outgrowth, was increased after ELF-EMF exposure. Moreover, the expression of transient receptor potential canonical 1 (TRPC1) was significantly up-regulated accompanied by increased the peak amplitude of intracellular calcium level induced by ELF-EMF. Furthermore, silencing TRPC1 expression eliminated the up-regulation of the proneural genes and the promotion of neuronal differentiation and neurite outgrowth induced by ELF-EMF. These results suggest that ELF-EMF exposure promotes the neuronal differentiation and neurite outgrowth of eNSCs via up-regulation the expression of TRPC1 and proneural genes (NeuroD and Ngn1). These findings also provide new insights in understanding the effects of ELF-EMF exposure on embryonic brain development.

(E) Maaroufi K, Ammari M, Elferchichi M, Poucet B, Sakly M, Save E, Abdelmelek H. Effects of combined ferrous sulphate administration and exposure to static magnetic field on spatial learning and motor abilities in rats. Brain Inj 27(4):492-499, 2013.(AS, CE, BE)

Primary objective: Occupational exposure to static magnetic fields (SMF) increases, in particular due to the widespread use of Magnetic Resonance Imaging (MRI) for medical diagnosis, thus raising health concerns. This study investigated the behavioural effects of 128 mT SMF in rats and examined the hypothesis that iron supplementation (3 mg kg(-1) for 5 days) potentiate the effects of SMF. **Methods:** Spatial learning abilities in the water maze, motor co-ordination in the rotarod and motor skills in the stationary beam and suspending string tests were assessed in iron-treated, SMF-exposed and co-exposed SMF-iron rats. **Results:** Acquisition of the water maze navigation task was unaffected in all groups. SMF-exposed and iron-treated rats showed a deficit in the 7-day retention test. No deficit was found in the rotarod and suspended string tests in all groups. Only iron-treated rats were impaired in the stationary beam test. A combination of iron and SMF treatments did not produce additional degradation of performance in all tests. **Conclusion:** SMF exposure had no massive effect but affected long-term spatial memory. Iron supplementation and 128 mT SMF had no synergistic effects.

(E) Madjid Ansari A, Farzampour S, Sadr A, Shekarchi B, Majidzadeh-A K. Effects of short term and long term Extremely Low Frequency Magnetic Field on depressive disorder in mice: Involvement of nitric oxide pathway. Life Sci. 146:52-57, 2016. (AS, AE, CE, BE, OX)

AIMS: Previous reports on the possible effects of Extremely Low Frequency Magnetic Fields (ELF MF) on mood have been paradoxical in different settings while no study has yet been conducted on animal behavior. In addition, it was shown that ELF MF exposure makes an increase in brain nitric oxide level. Therefore, in the current study, we aimed to assess the possible effect(s) of ELF MF exposure on mice Forced Swimming Test (FST) and evaluate the probable role of the increased level of nitric oxide in the observed behavior. MAIN METHODS: Male adult mice NMRI were recruited to investigate the short term and long term ELF MF exposure (0.5 mT and 50 Hz, single 2h and 2 weeks 2h a day). Locomotor behavior was assessed by using open-field test (OFT) followed by FST to evaluate the immobility time. Accordingly, NΩ-nitro-l-arginine methyl ester 30 mg/kg was used to exert anti-depressant like effect. KEY FINDINGS: According to the results, short term exposure did not alter the immobility time, whereas long term exposure significantly reduces immobility time ($p<0.01$). However, it was revealed that the locomotion did not differ among all experimental groups. Short term exposure reversed the anti-depressant like effect resulting from 30 mg/kg of NΩ-nitro-l-arginine methyl ester ($p<0.01$). SIGNIFICANCE: It has been concluded that long term exposure could alter the depressive disorder in mice, whereas short term exposure has no significant effect. Also, reversing the anti-depressant activity of L-NAME indicates a probable increase in the brain nitric oxide.

(E) Maes A, Anthonissen R, Wambacq S, Simons K, Verschaeve L. The Cytome Assay as a Tool to Investigate the Possible Association Between Exposure to Extremely Low Frequency Magnetic Fields and an Increased Risk for Alzheimer's Disease. J Alzheimers Dis. 50(3):741-749, 2016. (CS, AE, MC, ND)

Exposure to extremely low frequency magnetic fields (ELF-MF) has been identified as one of the potential environmental risk factors for Alzheimer's disease (AD). However, this is far from being established. So far there is no experimental evidence supporting this alleged association. We have performed an in vitro cytogenetic laboratory investigation to explore the plausibility of such association. Our investigation was based on possible similarities found in cells from AD patients and in cells exposed to ELF-MF. We especially found that 50 Hz ELF-MF increase the frequency of cells with (large) micronuclei and nuclear buds indicating that fields above 50 µT may induce chromosome instabilities as those found in AD patients. It should be stressed yet that results from the few published experimental studies on ELF-MF and AD are rather reassuring. Thus, our findings certainly do not prove anything. They only suggest that further investigations might be necessary.

(E) Maestú C, Blanco M, Nevado A, Romero J, Rodríguez-Rubio P, Galindo J, Bautista Lorite J, de las Morenas F, Fernández-Argüelles P. Reduction of pain thresholds in fibromyalgia after very low-intensity magnetic stimulation: a double-blinded, randomized placebo-controlled clinical trial. Pain Res Manag. 18(6):e101-106, 2013. (HU, BE, MA)

BACKGROUND: Exposure to electromagnetic fields has been reported to have analgesic and antinociceptive effects in several organisms. Objective: To test the effect of very low-intensity transcranial magnetic stimulation on symptoms associated with fibromyalgia syndrome. METHODS: A double-blinded, placebo-controlled clinical trial was performed in the Sagrado Corazón Hospital, Seville, Spain. Female fibromyalgia patients (22 to 50 years of age) were randomly assigned to either a stimulation group or a sham group. The stimulation group (n=28) was stimulated using 8 Hz pulsed magnetic fields of very low intensity, while the sham group (n=26) underwent the same protocol without stimulation. Pressure pain thresholds before and after stimulation were determined using an algometer during the eight consecutive weekly sessions of the trial. In addition, blood serotonin levels were measured and patients completed questionnaires to monitor symptom evolution. RESULTS: A repeated-measures ANOVA indicated statistically significant improvement in the stimulation group compared with the control group with respect to somatosensory pain thresholds, ability to perform daily activities, perceived chronic pain and sleep quality. While improvement in pain thresholds was apparent after the first stimulation session, improvement in the other three measures occurred after the sixth week. No significant between-group differences were observed in scores of depression, fatigue, severity of headaches or serotonin levels. No adverse side effects were reported in any of the patients. CONCLUSIONS: Very low-intensity magnetic stimulation may represent a safe and effective treatment for chronic pain and other symptoms associated with fibromyalgia.

(E) Mahdavi SM, Sahraei H, Yaghmaei P, Tavakoli H. Effects of Electromagnetic Radiation Exposure on Stress-Related Behaviors and Stress Hormones in Male Wistar Rats. Biomol Ther (Seoul). 22(6):570-576, 2014. (AS, AE, CE, CC, BE)

Studies have demonstrated that electromagnetic waves, as the one of the most important physical factors, may alter cognitive and non-cognitive behaviors, depending on the frequency and energy. Moreover, non-ionizing radiation of low energy waves e.g. very low frequency waves could alter this phenomenon via alterations in neurotransmitters and neurohormones. In this study, short, medium, and long-term exposure to the extremely low frequency electromagnetic field (ELF-EMF) (1 and 5 Hz radiation) on behavioral, hormonal, and metabolic changes in male Wistar rats (250 g) were studied. In addition, changes in plasma concentrations for two main stress hormones, noradrenaline and adrenocorticotropic hormone (ACTH) were evaluated. ELF-EMF exposure did not alter body weight, and food and water intake. Plasma glucose level was increased and decreased in the groups which exposed to the 5 and 1Hz wave, respectively. Plasma ACTH concentration increased in both using frequencies, whereas nor-adrenaline concentration showed overall reduction. At last, numbers of rearing, sniffing, locomotor activity was increased in group receiving 5 Hz wave over the time. In conclusions, these data showed that the effects of 1 and 5 Hz on the hormonal, metabolic and stress-like behaviors may be different. Moreover, the influence of waves on stress system is depending on time of exposure.

(E) Mahdavi SM, Sahraei H, Rezaei-Tavirani M, Najafi Abedi A. Common behaviors alterations after extremely low-frequency electromagnetic field exposure in rat animal model. Electromagn Biol Med. 35:222-227, 2016. (AS, CE, BE)

Naturally, the presence of electromagnetic waves in our living environment affects all components of organisms, particularly humans and animals, as the large part of their body consists of water. In the present study, we tried to investigate the relation between exposure to the extremely low-frequency electromagnetic field (ELF-EMF) and common behaviors such as body weight, food and water intake, anorexia (poor appetite), plasma glucose concentration, movement, rearing and sniffing in rats. For this purpose, rats were exposed to 40 Hz ELF-EMF once a day for 21 days, then at days 1, 3, 7, 14 and 21 after exposure, any changes in the above-mentioned items were assessed in the exposed rats and compared to the non-exposed group as control. Body weight of irradiated rats significantly increased only a week after exposure and decreased after that. No significant change was observed in food and water intake of irradiated rats compared to the control, and the anorexia parameter in the group exposed to ELF-EMF was significantly decreased at one and two weeks after irradiation. A week after exposure, the level of glucose was significantly increased but at other days these changes were not significant. Movements, rearing and sniffing of rats at day 1 after exposure were significantly decreased and other days these changes did not follow any particular pattern. However, the result of this study demonstrated that exposure to ELF-EMF can alter the normal condition of animals and may represent a harmful impact on behavior.

(E) Maldonado-Moreles A, Cordova-Fraga T, Bonilla-Jaime H, Lopez-Camacho PY, Basurto-Islas Low frequency vortex magnetic field reduces amyloid β aggregation, increase cell viability and protect from amyloid β toxicity. Electromagn Biol Med 40: 191-200, 2020. (CS, AE, CC)

Plaques formed by abnormal accumulation of amyloid β-peptide (Aβ) lead to onset of Alzheimer's disease (AD). Pharmacological treatments do not reduce Aβ aggregation neither restore learning and memory. Noninvasive techniques have emerged as an alternative to treat AD, such as stimulation with electromagnetic fields (EMF) that decrease Aβ deposition and reverses cognitive impairment in AD mice, even though some studies showed side effects on parallel magnetic fields stimulation. As a new approach of magnetic field (MF) stimulation, vortex magnetic fields (VMF) have been tested inducing a random movement of charged biomolecules in cells, promoting cell viability and apparently safer than parallel magnetic fields. In this study we demonstrate the effect of VMF on Aβ aggregation. The experimental strategy includes, i) design and construction of a coil capable to induce VMF, ii) evaluation of VMF stimulation on Aβ peptide induced-fibrils-formation, iii) evaluation of VMF stimulation on SH-SY5Y neuroblastoma cell line in the presence of Aβ peptide. We demonstrated for the first time that Aβ aggregation exposed to VMF during 24 h decreased ~ 86% of Aβ fibril formation compared to control. Likewise, VMF stimulation reduced Aβ fibrils-cytotoxicity and increase SH-SY5Y cell viability. These data establish the basis for future investigation that involve VMF as inhibitor of Aβ-pathology and indicate the therapeutic potential of VMF for AD treatment.

(E) Manikonda PK, Rajendra P, Devendranath D, Gunasekaran B, Channakeshava, Aradhya RS, Sashidhar RB, Subramanyam C. Influence of extremely low frequency magnetic fields on Ca2+ signaling and NMDA receptor functions in rat hippocampus. Neurosci Lett. 413(2):145-149, 2007. (AS, CE, CC)

Extremely low frequency (ELF<300Hz) electromagnetic fields affect several neuronal activities including memory. Because ELF magnetic fields cause altered Ca(2+) homeostasis in neural tissues, we examined their influence on Ca(2+) signaling enzymes in hippocampus and related them with NMDA receptor functions. Hippocampal regions were obtained from brains of 21-day-old rats that were exposed for 90 days to 50Hz magnetic fields at 50 and 100 microT intensities. In comparison to controls, ELF exposure caused increased intracellular Ca(2+) levels concomitant with increased activities of Ca(2+)-dependent protein kinase C (PKC), cAMP-dependent protein kinase and calcineurin as well as decreased activity of Ca(2+)-calmodulin-dependent protein kinase in hippocampal regions. Simultaneous ligand-binding studies revealed decreased binding to N-methyl-D-aspartic acid (NMDA) receptors. The combined results suggest that perturbed neuronal functions caused by ELF exposure may involve altered Ca(2+) signaling events contributing to aberrant NMDA receptor activities.

(E) Manikonda PK, Rajendra P, Devendranath D, Gunasekaran B, Channakeshava, Aradhya SR, Sashidhar RB, Subramanyam C. Extremely low frequency magnetic fields induce oxidative stress in rat brain. Gen Physiol Biophys. 33:81-90, 2014. (AS, CE, OX, CC)

The present investigation was conducted to understand the influence of long-term exposure of rats to extremely low frequency magnetic fields (ELF-MF), focusing on oxidative stress (OS) on different regions of rat's brain. Male Wistar rats (21-day-old) were exposed to ELF-MF (50 Hz; 50 and 100 µT) for 90 days continuously; hippocampal, cerebellar and cortical regions from rats were analyzed for (i) reactive oxygen species (ROS), (ii) metabolites indicative of OS and (iii) antioxidant enzymes. In comparison to control group rats, the rats that were continuously exposed to ELF-MF caused OS and altered glutathione (GSH/GSSG) levels in dose-dependent manner in all the regions of the brain. Accumulation of ROS, lipid peroxidation end products and activity of superoxide dismutase in different regions was in the descending order of cerebellum < hippocampus < cortex. Decrement in GSH/GSSG levels and increment in glutathione peroxidase activity were in the descending order of hippocampus < cerebellum < cortex. The continuous exposure to ELF-MF caused OS in all the examined regions of brain more significantly at 100 µT than at 50 µT. Varied influences observed in different regions of the brain, as documented in this study, may contribute to altered metabolic patterns in its related regions of the central nervous system, leading to aberrant neuronal functions.

(E) Manjhi J, Kumar S, Behari J, Mathur R. Effect of extremely low frequency magnetic field in prevention of spinal cord injury-induced osteoporosis. J Rehabil Res Dev. 50(1):17-30, 2013. (AS, CE, MA)

The present study was designed to investigate the effect of extremely low frequency (ELF) magnetic field (MF) on spinal cord injury (SCI)-induced osteoporosis in rats. Adult male Wistar rats (n = 24) were equally divided into sham, SCI, and SCI+MF groups. Complete transection of spinal cord (thoracic 11 vertebra) was surgically performed under anesthesia, whereas in the sham group only laminectomy was done. Post-SCI day 1, rats were either exposed (2 h/d × 8 wk) to ELF-MF (17.96 micro-Tesla, 50 Hz; SCI+MF group) or sham exposed (SCI group). Basso, Beattie, and Bresnahan (BBB) score was recorded weekly. All the rats were sacrificed 8 wk post-

SCI; tibia and femur bones were isolated for the analysis of bone mineral content (BMC; total calcium [Ca], phosphorus [P], carbon [C]), bone mineral density (BMD), and biochemical status (osteocalcin, collagen I, alkaline phosphatase). The BBB score decreased post-SCI, which partially recovered after ELF-MF. In SCI rats, there was a statistically significant decrease in BMC, Ca, P, C, BMD, and biochemical level in both the bones as compared with the sham group, which was attenuated in SCI+MF rats except the C content. Electron microscopic study revealed the enhancement of microstructural composition and compactness in cortical and trabecular parts of treated bones. The results suggest that the chronic (2 h/d × 8 wk) ELF-MF exposure (17.96 micro-Tesla, 50 Hz) to SCI rats is effective in attenuating SCI-induced osteoporosis.

(E) Marchesi N, Osera C, Fassina L, Amadio M, Angeletti F, Morini M, Magenes G, Venturini L, Biggiogera M, Ricevuti G, Govoni S, Caorsi S, Pascale A, Comincini S. Autophagy is modulated in human neuroblastoma cells through direct exposition to low frequency electromagnetic fields. J Cell Physiol. 229(11):1776-1786, 2014. (CS, AE, CC, ND, MA)

In neurogenerative diseases, comprising Alzheimer's (AD), functional alteration in autophagy is considered one of the pathological hallmarks and a promising therapeutic target. Epidemiological investigations on the possible causes undergoing these diseases have suggested that electromagnetic fields (EMF) exposition can contribute to their etiology. On the other hand, EMF have therapeutic implications in reactivating neuronal functionality. To partly clarify this dualism, the effect of low-frequency EMF (LF-EMF) on the modulation of autophagy was investigated in human neuroblastoma SH-SY5Y cells, which were also subsequently exposed to Aβ peptides, key players in AD. The results primarily point that LF-EMF induce a significant reduction of microRNA 30a (miR-30a) expression with a concomitant increase of Beclin1 transcript (BECN1) and its corresponding protein. Furthermore, LF-EMF counteract the induced miR-30a up-regulation in the same cells transfected with miR-30a mimic precursor molecules and, on the other side, rescue Beclin1 expression after BECN1 siRNA treatment. The expression of autophagy-related markers (ATG7 and LC3B-II) as well as the dynamics of autophagosome formation were also visualized after LF-EMF exposition. Finally, different protocols of repeated LF-EMF treatments were assayed to contrast the effects of Aβ peptides in vitro administration. Overall, this research demonstrates, for the first time, that specific LF-EMF treatments can modulate in vitro the expression of a microRNA sequence, which in turn affects autophagy via Beclin1 expression. Taking into account the pivotal role of autophagy in the clearance of protein aggregates within the cells, our results indicate a potential cytoprotective effect exerted by LF-EMF in neurodegenerative diseases such as AD.

Marchewka R, Trzmiel T, Hojan K. The Effect of Extremely Low-Frequency Magnetic Field on Stroke Patients: A Systematic Review. Brain Sci 14(5):430, 2024. (Review)

Background: The aim of this study was to review the current state of scientific evidence on the effect of extremely low-frequency magnetic fields stimulation (ELF-MFs) on stroke patients. **Methods:** A systematic review of PubMed, ScienceDirect, PeDro and Embase databases was conducted. Only articles published in English, involving adult participants and focusing on

individuals who had experienced a stroke, specifically examining the impact of ELF-MFs on post-stroke patients and had well-defined criteria for inclusion and exclusion of participants, were included. The methodological quality of the included studies was assessed using the Quality Assessment Tool for Quantitative Studies (QATQS). **Results:** A total of 71 studies were identified through database and reference lists' search, from which 9 were included in the final synthesis. All included studies showed a beneficial effect of ELF-MFs on stroke patients, however seven of the included studies were carried by the same research group. Improvements were observed in domains such as oxidative stress, inflammation, ischemic lesion size, functional status, depressive symptoms and cognitive abilities. **Conclusions:** The available literature suggests a beneficial effect of ELF-MFs on post-stroke patients; however, the current data are too limited to broadly recommend the use of this method. Further research with improved methodological quality is necessary.

Martel J, Chang SH, Chevalier G, Ojcius DM, Young JD. Influence of electromagnetic fields on the circadian rhythm: Implications for human health and disease. Biomed J. 46(1):48-59, 2023. (opinion)

Living organisms have evolved within the natural electromagnetic fields (EMFs) of the earth which comprise the global atmospheric electrical circuit, Schumann resonances (SRs) and the geomagnetic field. Research suggests that the circadian rhythm, which controls several physiological functions in the human body, can be influenced by light but also by the earth's EMFs. Cyclic solar disturbances, including sunspots and seasonal weakening of the geomagnetic field, can affect human health, possibly by disrupting the circadian rhythm and downstream physiological functions. Severe disruption of the circadian rhythm increases inflammation which can induce fatigue, fever and flu-like symptoms in a fraction of the population and worsen existing symptoms in old and diseased individuals, leading to periodic spikes of infectious and chronic diseases. Possible mechanisms underlying sensing of the earth's EMFs involve entrainment via electrons and electromagnetic waves, light-dependent radical pair formation in retina cryptochromes, and paramagnetic magnetite nanoparticles. Factors such as electromagnetic pollution from wireless devices, base antennas and low orbit internet satellites, shielding by non-conductive materials used in shoes and buildings, and local geomagnetic anomalies may also affect sensing of the earth's EMFs by the human body and contribute to circadian rhythm disruption and disease development.

Martel J, Rouleau N, Murugan NJ, Chin WC, Ojcius DM, Young JD.Effects of light, electromagnetic fields and water on biological rhythms. Biomed J 2024 Dec 11:100824. doi: 10.1016/j.bj.2024.100824. Online ahead of print. (Review)

The circadian rhythm controls a wide range of functions in the human body and is required for optimal health. Disruption of the circadian rhythm can produce inflammation and initiate or aggravate chronic diseases. The modern lifestyle involves long indoor hours under artificial lighting conditions as well as eating, working, and sleeping at irregular times, which can disrupt the circadian rhythm and lead to poor health outcomes. Seasonal solar variations, the sunspot cycle and anthropogenic electromagnetic fields can also influence biological rhythms. The possible mechanisms underlying these effects are discussed, which include resonance, radical-

pair formation in retina cryptochromes, ion cyclotron resonance, and interference, ultimately leading to variations in melatonin and cortisol. Intracellular water, which represents a coherent, ordered phase that is sensitive to infrared light and electromagnetic fields, may also respond to solar variations and man-made electromagnetic fields. We describe here various factors and underlying mechanisms that affect the regulation of biological rhythms, with the aim of providing practical measures to improve human health

(E) Martínez-Sámano J, Torres-Durán PV, Juárez-Oropeza MA, Verdugo-Díaz L. Effect of acute extremely low frequency electromagnetic field exposure on the antioxidant status and lipid levels in rat brain. Arch Med Res. 43(3):183-189, 2012. (AS, AE, CC, OX)

BACKGROUND AND AIMS: It is generally accepted that electromagnetic fields (EMF) can exert biological effects; however, the mechanisms by which EMF elicits responses are still unknown. The present study was designed to assess the immediate effects of acute EMF exposure, movement restriction, and the combination of both on the antioxidant systems and lipid content in the whole brain of rat. METHODS: Thirty two male Wistar rats were arranged in four groups: control, EMF exposed, movement restrained (MR), and EMF + MR for 2 h. Rats were then sacrificed and their brains analyzed for superoxide dismutase and catalase activities, reduced glutathione, nitric oxide, total cholesterol, and triacylglycerol levels, as well as plasma corticosterone concentrations. RESULTS: Acute exposure to EMF induces reduction in catalase and superoxide dismutase activities, whereas the combination of EMF + MR also decreases both reduced glutathione and nitric oxide levels. Our results show that the acute exposure to EMF does not induce elevation of stress-hormone corticosterone but impairs the antioxidant status in rat brain. CONCLUSIONS: Plasma corticosterone concentration and antioxidant data indicate that the acute exposure to EMF appears to be a mild stressor that leads to some adaptive responses due to the activation of systems controlling the brain oxidative balance.

(E) Masoudian N, Riazi GH, Afrasiabi A, Modaresi SM, Dadras A, Rafiei S, Yazdankhah M, Lyaghi A, Jarah M, Ahmadian S, Seidkhani H. Variations of Glutamate Concentration Within Synaptic Cleft in the Presence of Electromagnetic Fields: An Artificial Neural Networks Study. Neurochem Res. 40(4):629-642, 2015. (CS, AE, CC, MA)

Glutamate is an excitatory neurotransmitter that is released by the majority of central nervous system synapses and is involved in developmental processes, cognitive functions, learning and memory. Excessive elevated concentrations of Glu in synaptic cleft results in neural cell apoptosis which is called excitotoxicity causing neurodegenerative diseases. Hence, we investigated the possibility of extremely low frequency electromagnetic fields (ELF-EMF) as a risk factor which is able to change Glu concentration in synaptic clef. Synaptosomes as a model of nervous terminal were exposed to ELF-EMF for 15-55 min in flux intensity range from 0.1 to 2 mT and frequency range from 50 to 230 Hz. Finally, all raw data by INForm v4.02 software as an artificial neural network program was analyzed to predict the effect of whole mentioned range spectra. The results showed the tolerance of all effects between the ranges from -35 to +40 % compared to normal state when glutamatergic systems exposed to ELF-EMF. It indicates that glutamatergic system attempts to compensate environmental changes though release or reuptake in order to keep the system safe. Regarding the wide range of ELF-EMF acquired in this study, the obtained outcomes have potential for developing treatments based on ELF-EMF for some

neurological diseases; however, in vivo experiments on the cross linking responses between glutamatergic and cholinergic systems in the presence of ELF-EMF would be needed.
No DNA damage response and negligible genome-wide transcriptional changes in human embryonic stem cells exposed to terahertz radiation.

(E)

Mastrodonato A, Barbati SA, Leone L, Colussi C, Gironi K, Rinaudo M, Piacentini R, Denny CA, Grassi C. Olfactory memory is enhanced in mice exposed to extremely low-frequency electromagnetic fields via Wnt/β-catenin dependent modulation of subventricular zone neurogenesis. Sci Rep 8(1):262, 2018. ***(AS, CE, BE)***

Exposure to extremely low-frequency electromagnetic fields (ELFEF) influences the expression of key target genes controlling adult neurogenesis and modulates hippocampus-dependent memory. Here, we assayed whether ELFEF stimulation affects olfactory memory by modulating neurogenesis in the subventricular zone (SVZ) of the lateral ventricle, and investigated the underlying molecular mechanisms. We found that 30 days after the completion of an ELFEF stimulation protocol (1 mT; 50 Hz; 3.5 h/day for 12 days), mice showed enhanced olfactory memory and increased SVZ neurogenesis. These effects were associated with upregulated expression of mRNAs encoding for key regulators of adult neurogenesis and were mainly dependent on the activation of the Wnt pathway. Indeed, ELFEF stimulation increased Wnt3 mRNA expression and nuclear localization of its downstream target β-catenin. Conversely, inhibition of Wnt3 by Dkk-1 prevented ELFEF-induced upregulation of neurogenic genes and abolished ELFEF's effects on olfactory memory. Collectively, our findings suggest that ELFEF stimulation increases olfactory memory via enhanced Wnt/β-catenin signaling in the SVZ and point to ELFEF as a promising tool for enhancing SVZ neurogenesis and olfactory function.

(NE) Masuda H, de Gannes FP, Haro E, Billaudel B, Ruffié G, Lagroye I, Veyret B. Lack of effect of 50-Hz magnetic field exposure on the binding affinity of serotonin for the 5-HT 1B receptor subtype. Brain Res. 1368:44-51, 2011. (CS, AE, CC)

There is some concern that exposure to extremely low-frequency magnetic fields (MF) causes adverse health effects via signal transduction pathways. Two previous studies reported that exposure to 50-Hz MF decreased the binding affinity of the 1B receptor subtype of serotonin (5-HT) in rat brain membranes. The aim of this study was to investigate whether the exposure to MF affects binding to the 5-HT(1B) receptor and a physiological function associated with 5-HT(1B) receptor activation. Rat brain crude membrane fractions, including 5-HT(1B) receptor and C6-glial cells transfected with human 5-HT(1B) receptor gene, were exposed to 50-Hz MF at 1 mT using Merritt coils under temperature-regulated conditions. In the rat crude membrane, there was no significant difference in the affinity constant of [(3)H]-5-HT between exposed (K(d): 0.92±0.38 nM) and sham-exposed (K(d): 1.00±0.32 nM). The lack of affinity change after exposure was also confirmed using a chemical agonist of the 5-HT receptor, [(3)H]-5-carboxytryptamine (K(d): 0.59±0.06 nM for exposed and 0.71±0.08 nM for sham). Similar negative results in terms of affinity constant were obtained on the human 5-HT(1B) receptor in C6-glial cells. In addition, forskolin-stimulated cAMP production was inhibited by 5-HT

administration in a dose-dependent manner in C6-glial cells, but exposure did not modify the inhibitory response. This study thus failed to confirm the previous results and findings suggest that exposure to MF below the current occupational limit does not affect the physiological function involved in 5-HT(1B) receptor subtypes.

(E) Medina-Fernandez FJ, Escribano BM, Agüera E, Aguilar-Luque M, Feijoo M, Luque E, Garcia-Maceira FI, Pascual-Leone A, Drucker-Colin R, Tunez I. Effects of transcranial magnetic stimulation on oxidative stress in experimental autoimmune encephalomyelitis. Free Radic Res. 2017 May;51(5):460-469, 2017. (AS, CE, MC, OX, ND, MA)

Experimental autoimmune encephalomyelitis (EAE) reproduces a multiple sclerosis (MS)-like experimental model. The main objective was to evaluate the effect of extremely low-frequency electromagnetic fields (EL-EMF) application, like a paradigm of transcranial magnetic stimulation (TMS) in the development of EAE. Rats were injected with a single dose of 150 µg of myelin oligodendrocyte glycoprotein (MOG, fragment 35-55) to produce experimental MS. To assess the effect of TMS application in EAE, the rats were treated with TMS (60 Hz and 0.7 mT) for 2 h in the morning, once a day, 5 days a week, during 3 weeks. TMS was applied to the head. The effect of TMS on EAE was evaluated as motor symptoms and, oxidative and cell damage. The data showed that MOG induced motor symptoms as tail paralysis and limb paresis/paralysis, oxidative stress and cell death similar to MS when compared with control animals. Importantly, TMS application attenuated motor symptoms, oxidative and cell damage, whereas it increased antioxidant system. Our findings suggest that: (i) MOG reproduces an experimental model of MS characterised by oxidative and cell damage; and (ii) TMS application decreases oxidative stress and cell death induced by MOG.

(E) Metto AC, Telgkamp P, McLane-Svoboda AK, Gilad AA, Pelled G. Closed-loop neurostimulation via expression of magnetogenetics-sensitive protein in inhibitory neurons leads to reduction of seizure activity in a rat model of epilepsy. Brain Res 1820:148591, 2023. (CS, AE, CC, FC, MA)

On-demand neurostimulation has shown success in epilepsy patients with pharmacoresistant seizures. Seizures produce magnetic fields that can be recorded using magnetoencephalography. We developed a new closed-loop approach to control seizure activity based on magnetogenetics using the electromagnetic perceptive gene (EPG) that encodes a protein that responds to magnetic fields. The EPG transgene was expressed in inhibitory interneurons under the hDlx promoter and kainic acid was used to induce acute seizures. In vivo electrophysiological signals were recorded. We found that hDlx EPG rats exhibited a significant delay in the onset of first seizure (1142.72 ± 186.35 s) compared to controls (644.03 ± 15.06 s) and significantly less seizures (4.11 ± 1.03) compared to controls (8.33 ± 1.58). These preliminary findings suggest that on-demand activation of EPG expressed in inhibitory interneurons suppresses seizure activity, and magnetogenetics via EPG may be an effective strategy to alleviate seizure severity in a closed-loop, and cell-specific fashion.

(E) Monazzam MR, Hosseini M, Matin LF, Aghaei HA, Khosroabadi H, Hesami A. Sleep quality and general health status of employees exposed to extremely low frequency magnetic fields

in a petrochemical complex. Journal of Environmental Health Science and Engineering 12**:78, 2014. (CE, HU, BE)**

Background. Advances in science and technology of electrical equipment, despite increasing human welfare in everyday life, have increased the number of people exposed to Electro-Magnetic Fields (EMFs). Because of possible adverse effects on the health of exposed individuals, the EMFs have being the center of attention. This study was performed to determine possible correlation between Extremely Low Frequency Electro-Magnetic Fields (ELF EMFs) and sleep quality and public health of those working in substation units of a petrochemical complex in southern Iran. Materials and method. To begin with, magnetic flux density was measured at different parts of a Control Building and two substations in accordance with IEEE std 644 1994. Subsequently, the questionnaires Pittsburgh Sleep Quality Index (PSQI) and General Health Quality (GHQ) were used to investigate relationship between ELF exposure level and sleep quality and public health, respectively. Both questionnaires were placed at disposal of a total number of 40 workers at the complex. The filled out questionnaires were analyzed by T-test, Duncan and the Chi-square tests. Results. The obtained results revealed that 28% of those in case group suffered from poor health status and 61% were diagnosed with a sleep disorder. However, all members in control group were in good health condition and only 4.5% of them had undesirable sleep quality. Conclusion. In spite of a significant difference between the case and control groups in terms of sleep quality and general health, no significant relationship was found between the exposure level and sleep quality and general health. It is worth noting that the measured EMF values were lower than the standard limits recommended by American Conference of Industrial Hygienists (ACGIH). However, given the uncertainties about the pathogenic effects caused by exposure to ELF EMFs, further epidemiological studies and periodic testing of personnel working in high voltage substations are of utmost importance.

(E) Moya-Gómez A, Font LP, Burlacu A, Alpizar YA, Cardonne MM, Brône B, Bronckaers A.
Extremely Low-Frequency Electromagnetic Stimulation (ELF-EMS) Improves Neurological Outcome and Reduces Microglial Reactivity in a Rodent Model of Global Transient Stroke. Int J Mol Sci 24(13):11117, 2023. (AS, CS, CE, MC, BE, MA, ND)

Extremely low-frequency electromagnetic stimulation (ELF-EMS) was demonstrated to be significantly beneficial in rodent models of permanent stroke. The mechanism involved enhanced cerebrovascular perfusion and endothelial cell nitric oxide production. However, the possible effect on the neuroinflammatory response and its efficacy in reperfusion stroke models remains unclear. To evaluate ELF-EMS effectiveness and possible immunomodulatory response, we studied neurological outcome, behavior, neuronal survival, and glial reactivity in a rodent model of global transient stroke treated with 13.5 mT/60 Hz. Next, we studied microglial cells migration and, in organotypic hippocampal brain slices, we assessed neuronal survival and microglia reactivity. ELF-EMS improved the neurological score and behavior in the ischemia-reperfusion model. It also improved neuronal survival and decreased glia reactivity in the hippocampus, with microglia showing the first signs of treatment effect. In vitro ELF-EMS

decreased (Lipopolysaccharide) LPS and ATP-induced microglia migration in both scratch and transwell assay. Additionally, in hippocampal brain slices, reduced microglial reactivity, improved neuronal survival, and modulation of inflammation-related markers was observed. Our study is the first to show that an EMF treatment has a direct impact on microglial migration. Furthermore, ELF-EMS has beneficial effects in an ischemia/reperfusion model, which indicates that this treatment has clinical potential as a new treatment against ischemic stroke.

(E) Murugan NJ, Persinger MA. Comparisons of Responses by Planarian to Micromolar to Attomolar Dosages of Morphine or Naloxone and/or Weak Pulsed Magnetic Fields: Revealing Receptor Subtype Affinities and Nonspecific Effects. Int J Radiat Biol. 90:833-840, 2014. (AS, AE, BE)

Purpose: The behavioral responses of planaria to the exposures of a range of concentrations of morphine (µM to attoM) or the µ-opiate antagonist naloxone or to either of these compounds and a burst-firing magnetic field (5 µT) were studied. Material and Methods: The locomotor velocity (LMV) of planaria was measured after individual worms were exposed to increasing concentrations from attomolar to micromolar of morphine or naloxone, physiologically patterned magnetic fields or a combination of the two. Results: Compared to spring water controls, the two-hour exposure to the patterned magnetic field before measurement reduced activity by about 50% which was comparable to the non-specific effects of morphine and naloxone across all dosages except 1 attomolar that did not differ from spring water. The specific dosage of 100 nM produced additional marked reduction in activity for planaria exposed to either morphine or naloxone while only 1 pM of morphine produced this effect. Conclusion: The results support the presence of at least two receptor subtypes that mediate the diminished activity effects elicited by morphine specifically and suggests that exposure to the specifically patterned magnetic field produces a behavioral suppression whose magnitude is similar to the "dose independent" effects from this opiate.

(E) Navarro EA, Navarro-Modesto E. A mathematical model and experimental procedure to analyze the cognitive effects of audio frequency magnetic fields. Front Hum Neurosci 17:1135511, 2023. (HU, AE, BE)

Audio frequency magnetic fields (20 Hz-20 kHz) are magnetic fields in extremely low frequency-very low frequency (ELF-VLF) bands that are present near audio equipment and acoustic transducers. These devices transform and operate the electrical signal from the recordings or other devices into acoustic and audio signals. The cognitive influence of sound and noise has been widely studied and recognized since the times of ancient Rome; however, the cognitive effects of the magnetic fields of these frequencies have not been studied. Due to the extensive use of audio devices that use this type of transducer near the temporal-parietal area, we believe that it is of interest to study their impact on short-term memory or working memory (WM) and to analyze their potential as they operate as a transcranial magnetic stimulation. In this study, a mathematical model and an experimental tool are introduced to analyze memory performance. The model dissociates the reaction time of a cognitive task. We analyze the model in data from a group of 65 young, healthy subjects. WM is assessed in our experimental setup by means of the Sternberg test (ST), whereby during the ST, one subgroup was exposed to an audio

frequency magnetic stimulus, and the other subgroup received a sham stimulus. The magnetic stimulus was ~0.1 μT and was applied to both sides of the head at the frontal cortex near the temporal-parietal area, which is where WM is expected to be located. The ST records reaction times when determining whether an object displayed on the computer screen is one of the objects to be remembered. The results are analyzed within the mathematical model and changes are observed, including the deterioration of WM, which could affect 32% of its operability.

(E)Nemati M, Nozari M, Darvishzadeh-Mahani F, Ahmadi-Zeidabadi M, Ganjalikhan-Hakemi S, Bashiri H, Haratizadeh S. Expression Pattern Alterations of the Brain KCC2 Chloride Transporter in Male Rats Following Postnatal Extremely Low-Frequency Electromagnetic Field Exposure Associated With Behavioral Outcomes. Birth Defects Res. 117(11):e2546, 2025. (AS, CE, CC, BE, OX, DE)

Background: Exposure to extremely low-frequency magnetic fields (ELF-MFs) has increased with technological development. Environmental factors are known to influence the K^+-Cl^- cotransporter 2 (KCC2), which regulates neuronal chloride homeostasis and is essential for brain development through its role in the GABAergic shift. In this study, we investigated the effects of ELF-MF exposure on KCC2 expression and related behavioral and biochemical outcomes in Wistar rat pups. **Methods:** Wistar rat pups were exposed to ELF-MF (10 mT, 50 Hz) for 2 h per day from postnatal day (PND) 1 to 10. **Results:** Results indicated a significant reduction in KCC2 expression in the ELF-MF-exposed group. Furthermore, these animals exhibited enhanced anxiety-like behaviors, elevated brain malondialdehyde (MDA) levels, and shortened latency to tonic-clonic seizures compared with controls. **Conclusions:** These findings suggest that early exposure to ELF-MFs disrupts KCC2 expression in the developing brain and induces behavioral and biochemical abnormalities in male rats.

(E) Nishimura T, Tada H, Fukushima M. Correlation between the Lunar Phase and Tail-Lifting Behavior of Lizards (*Pogona vitticeps*) Exposed to an Extremely Low-Frequency Electromagnetic Field. Animals (Basel). 9(5). pii: E208, 2019. (AS, CE, BE)

We previously showed that the agamid lizard *Pogona vitticeps* responded to an extremely low-frequency electromagnetic field (ELF-EMF; frequency: 6 and 8 Hz; peak magnetic field: 2.6 μT; peak electric field: 10 V/m) with tail-lifting behavior. In addition, the tail-lifting response to ELF-EMF disappeared when the parietal eyes of the lizards were covered by small round aluminum caps. This result suggests that the parietal eye contributes to light-dependent magnetoreception. In the present study, we set up an ELF-EMF group to evaluate the long-term effect of the ELF-EMF on lizards' behavior and examine our hypothesis that exposure to ELF-EMFs increases the magnetic field sensitivity in lizards. We therefore include the lunar phase (full moon/new moon) and K index as environmental factors related to the geomagnetic field in the analysis. The number of tail lifts per individual per day was the response variable while calendar month, daily mean temperature, daily mean humidity, daily mean atmospheric pressure, full moon, new moon, and K index were the explanatory variables. We analyzed an ELF-EMF group and a control group separately. In a multiple linear regression analysis, the independent determinants associated with the number of tail lifts were the full moon, the temperature, February, March, April, and May in the ELF-EMF group and March,

April, May, and June in the control group. The *P. vitticeps* in the ELF-EMF group responded to the full moon whereas those in the control group did not. In addition, in the ELF-EMF group, the number of tail lifts was higher on days when the K index was higher ($P = 0.07$) in the first period whereas there was no such tendency in either period in the control group. There is the possibility that the exposure to ELF-EMFs may increase magnetic-field sensitivity in lizards.

(E) Nordmann GC, Balay SD, Kapuruge TN, Numi M, Leeb C, Nimpf S, Malkemper EP, Landler L, Keays DA. A global screen for magnetically induced neuronal activity in the pigeon brain. Science. 2025 Nov 20:eaea6425. (AS, AE, EE)

How animals detect the Earth's magnetic field remains a mystery in sensory biology. Despite extensive behavioral evidence, the neural circuitry and molecular mechanisms responsible for magnetic sensing remain elusive. Adopting an unbiased approach we employ whole brain activity mapping, tissue clearing, and light sheet microscopy to identify neuronal populations activated by magnetic stimuli in the pigeon (*Columba livia*). We demonstrate robust, light-independent bilateral neuronal activation in the medial vestibular nuclei and the caudal mesopallium. Single-cell RNA sequencing of the semicircular cristae revealed specialized type II hair cells that express the molecular machinery necessary for the detection of magnetic stimuli by electromagnetic induction. Our data supports a model whereby electro-magnetic input from the semicircular canals activates a vestibular-mesopallial circuit within the pigeon brain.

Ohayon MM, Stolc V, Freund FT, Milesi C, Sullivan SS. The potential for impact of man-made super low and extremely low frequency electromagnetic fields on sleep. Sleep Med Rev. 47:28-38, 2019. (Review)

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An ever-growing number of electromagnetic (EM) emission sources elicits health concerns, particularly stemming from the ubiquitous low to extremely low frequency fields from power lines and appliances, and the radiofrequency fields emitted from telecommunication devices. In this article we review the state of knowledge regarding possible impacts of electromagnetic fields on melatonin secretion and on sleep structure and the electroencephalogram of humans. Most of the studies on the effects of melatonin on humans have been conducted in the presence of EM fields, focusing on the effects of occupational or residential exposures. While some of the earlier studies indicated that EM fields may have a suppressive effect on melatonin, the results cannot be generalized because of the large variability in exposure conditions and other factors that may influence melatonin. For instance, exposure to radiofrequency EM fields on sleep architecture show little or no effect. However, a number of studies show that pulsating radiofrequency electromagnetic fields, such as those emitted from cellular phones, can alter brain physiology, increasing the electroencephalogram power in selective bands when administered immediately prior to or during sleep. Additional research is necessary that would include older populations and evaluate the interactions of EM fields in different frequency ranges to examine their effects on sleep in humans.

(E) Ozdemir E, Demirkazik A, Gursoy S, Taskıran AS, Kilinc O, Arslan G. Effects of extremely low frequency electromagnetic fields on morphine analgesia and tolerance in rats. Gen Physiol Biophys. 36:415-422, 2017. (AS, CE, BE)

Several studies have demonstrated that the electromagnetic fields produce analgesic activity. The aim of this study was to investigate the effects of extremely low frequency (ELF) electromagnetic fields (EMF) on morphine analgesia and tolerance in rats. In the study, 78 adult male Wistar albino rats (approximately 240 ± 12 g) were used. The application of 50 Hz magnetic field, each day the same times for 30 minutes for 15 days, and a total of four times every 15 minute intervals. To constitute morphine tolerance, high dose of morphine (50 mg/kg) were administered for 3 days in rats and tolerance was evaluated on day 4. Prior to analgesia tests, the effective dose (5 mg/kg) of morphine was injected into rats. In the statistical analyzes of the data, analysis of variance (two-way ANOVA) was used and the multiple comparison determined by Tukey tests. The maximum analgesic effect of the 5 mT magnetic field was determined on 7 days. Administration of morphine (5 mg/kg) in rats exposed to a magnetic field, the analgesic effect was significantly higher compared to the morphine group ($p < 0.05$). Morphine tolerant animals exposed to a magnetic field, the analgesic effect was found significantly higher than morphine tolerant group rats ($p < 0.05$). Analgesia test data demonstrated that application of ELF-EMFs to rats increases the morphine analgesia and reduces morphine tolerance.

(E) Ozdemir E, Demirkazik A, Taskıran AS, Arslan G. Effects of 5-HT$_1$ and 5-HT $_2$ Receptor Agonists on Electromagnetic Field-Induced Analgesia in Rats. Bioelectromagnetics. 40(5):319-330, 2019. (AS, CE, CC, BE)

Much evidence demonstrates the antinociceptive effect of magnetic fields (MFs). However, the analgesic action mechanism of the electromagnetic field (EMF) is not exactly understood. The aim of the present study was to investigate the effects of 5-HT$_1$ and 5-HT$_2$ receptor agonists (serotonin HCl and 2,5-dimethoxy-4-iodoamphetamine [DOI] hydrochloride) on EMF-induced analgesia. In total, 66 adult male Wistar albino rats with an average body mass of 225 ± 13 g were used in this study. The animals were subjected to repeated exposures of alternating 50 Hz and 5 mT EMF for 2 h a day for 15 days. Prior to analgesia tests, serotonin HCl (5-HT$_1$ agonist) 4 mg/kg, WAY 100635 (5-HT$_1$ antagonist) 0.04 mg/kg, DOI hydrochloride (5-HT$_2$ receptor agonist) 4 mg/kg, and SB 204741 (5-HT$_2$ antagonist) 0.5 mg/kg doses were injected into rats. For statistical analysis of the data, analysis of variance was used and multiple comparisons were determined by Tukey's test. Administration of serotonin HCl MF (5 mT)-exposed rats produced a significant increase in percent maximal possible effect (% MPE) as compared with EMF group ($P < 0.05$). On the contrary, injection of WAY 100635 to MF-exposed rats produced a significant decrease in analgesic activity ($P < 0.05$). Similarly, the administration of DOI hydrochloride significantly increased % MPE values as compared with the EMF group while SB 204741 reduced it ($P < 0.05$). In conclusion, our results suggested that serotonin 5-HT$_1$ and 5-HT$_2$ receptors play an important role in EMF-induced analgesia; however, further research studies are necessary to understand the mechanism.

(E) Özgün A, Marote A, Behie LA, Salgado A, Garipcan B. Extremely low frequency magnetic field induces human neuronal differentiation through NMDA receptor activation. J Neural Transm (Vienna). 126(10):1281-1290, 2019. (CS, CE, CC, MC)

Magnetic fields with different frequency and intensity parameters exhibit a wide range of effects

on different biological models. Extremely low frequency magnetic field (ELF MF) exposure is known to augment or even initiate neuronal differentiation in several in vitro and in vivo models. This effect holds potential for clinical translation into treatment of neurodegenerative conditions such as autism, Parkinson's disease and dementia by promoting neurogenesis, non-invasively. However, the lack of information on underlying mechanisms hinders further investigation into this phenomenon. Here, we examine involvement of glutamatergic Ca2+ channel, N-methyl-D-aspartate (NMDA) receptors in the process of human neuronal differentiation under ELF MF exposure. We show that human neural progenitor cells (hNPCs) differentiate more efficiently under ELF MF exposure in vitro, as demonstrated by the abundance of neuronal markers. Furthermore, they exhibit higher intracellular Ca2+ levels as evidenced by c-fos expression and more elongated mature neurites. We were able to neutralize these effects by blocking NMDA receptors with memantine. As a result, we hypothesize that the effects of ELF MF exposure on neuronal differentiation originate from the effects on NMDA receptors, which sequentially triggers Ca2+-dependent cascades that lead to differentiation. Our findings identify NMDA receptors as a new key player in this field that will aid further research in the pursuit of effect mechanisms of ELF MFs.

(E) Packmor F, Kishkinev D, Zechmeister T, Mouritsen H, Holland RA. Migratory birds can extract positional information from magnetic inclination and magnetic declination alone. Proc Biol Sci 291(2034):rspb20241363, 2024. (AS, AE, BE)

Migratory birds are able to navigate over great distances with remarkable accuracy. The mechanism they use to achieve this feat is thought to involve two distinct steps: locating their position (the 'map') and heading towards the direction determined (the 'compass'). For decades, this map-and-compass concept has shaped our perception of navigation in animals, although the nature of the map remains debated. However, some recent studies suggest the involvement of the Earth's magnetic field in the map step. Here, we tested whether migratory songbirds, Eurasian reed warblers (*Acrocephalus scirpaceus*), can determine their position based on two magnetic field components that are also associated with direction finding, i.e. magnetic inclination and magnetic declination. During a virtual magnetic displacement experiment, the birds were exposed to altered magnetic inclination and magnetic declination values that would indicate a displacement from their natural migratory corridor, but the total intensity of the field remained unchanged, creating a spatial mismatch between these components. The response was a change in the birds' migratory direction consistent with a compensatory re-orientation. This suggests that birds can extract positional as well as directional information from these cues, even when they are in conflict with another component of the magnetic field. It remains to be seen whether birds use the total intensity of Earth's magnetic field for navigation.

(E) Park, H-J, J-H Choi, M-H. Nam, and Y-K. Seo. Induced neurodifferentiation of hBM-MSCs through activation of the ERK/CREB pathway via pulsed electromagnetic fields and physical stimulation promotes neurogenesis in cerebral ischemic models. Int. J. Mol. Sci 23:1177, 2022. (AS, CS, CE, MC, CC, BE, MA)

Stroke is among the leading causes of death worldwide, and stroke patients are more likely to live with permanent disabilities even after treatment. Several treatments are being developed to improve the quality of life of patients; however, these treatments still have important limitations.

Our study thus sought to evaluate the neural differentiation of human bone marrow mesenchymal stem cells (hBM-MSCs) at various pulsed electromagnetic field (PEMF) frequencies. Furthermore, the effects of selected frequencies in vivo were also evaluated using a mouse ischemia stroke model. Cell proliferation decreased by 20% in the PEMF group, as demonstrated by the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) assay, and lactate dehydrogenase (LDH) secretion increased by approximately 10% in an LDH release assay. Fluorescence-activated cell sorting (FACS) analysis demonstrated that CD73 and CD105 were downregulated in the PEMF group at 60 Hz. Moreover, microtubule-associated protein 2 (MAP-2) and neurofilament light chain (NF-L) were upregulated in cell cultures at 60 and 75 Hz. To assess the effects of PEMF in vivo, cerebral ischemia mice were exposed to a PEMF at 60 Hz. Neural-related proteins were significantly upregulated in the PEMF groups compared with the control and cell group. Upon conducting rotarod tests, the cell/PEMF group exhibited significant differences in motor coordination at 13 days post-treatment when compared with the control and stem-cell-treated group. Furthermore, the cell and cell/PEMF group exhibited a significant reduction in the expression of matrix metalloproteinase-9 (MMP-9), tumor necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ) in the induced ischemic area compared with the control. Collectively, our findings demonstrated that PEMFs at 60 and 75 Hz could stimulate hBM-MSCs neural differentiation in vitro, in addition to promoting neurogenesis to enhance the functional recovery process by reducing the post-stroke inflammatory reaction.

(E) Partsvania B, Sulaberidze T, Modebadze Z, Shoshiashvili L. Extremely low-frequency magnetic fields effects on the snail single neurons. Electromagn Biol Med. 27(4):409-417, 2008. (CS, EE)

The aim of present work is to explore the influence of extremely low-frequency electromagnetic fields (8.34 and 217 Hz) utilized in cell phones on habituation of the mollusk single neuron to intracellular stimuli. The isolated nervous system of the mollusk Helix Pomatia was used in the experiments. Helmholtz coils were used to expose brain ganglia to the low-frequency electromagnetic fields. Peak values of the extremely low-frequency fields were between 1 and 6 mT. Neuron electrophysiology was investigated using a standard microelectrode technique. Exposure of the neuron to the low-frequency electromagnetic fields caused dehabituation to intracellular stimulus. The effect was proportional to the magnetic induction peak value. The observed dehabituation occurs by degradation of the signal to noise ratio and by alteration of the neuron's normal function.

(E) Pedersen C, Poulsen AH, Rod NH, Frei P, Hansen J, Grell K, Raaschou-Nielsen O, Schüz J, Johansen C. Occupational exposure to extremely low-frequency magnetic fields and risk for central nervous system disease: an update of a Danish cohort study among utility workers. Int Arch Occup Environ Health. 90:619-628, 2017. (HU, CE, ND)

PURPOSE: Evidence of whether exposure to extremely low-frequency magnetic fields (ELF-MF) is related to central nervous system diseases is inconsistent. This study updates a previous study of the incidence of such diseases in a large cohort of Danish utility workers by almost doubling the period of follow-up. METHODS: We investigated

the risks for dementia, motor neurone disease, Parkinson disease, multiple sclerosis and epilepsy among 32,006 men employed at the 99 utility companies that supplied Denmark with electricity during the period 1900-1993. Cases were identified in the Danish National Patient Registry and the cohort was followed during 1982-2010. Exposure was estimated from a job-exposure matrix based on company records of job title and area of work and cohort members were allocated to one of three categories (<0.1, 0.1-0.99 and ≥1.0 μT). RESULTS: For dementia, multiple sclerosis and epilepsy the incidence rate ratios (IRR) were close to unity, but higher for motor neurone disease [IRR 1.24, 95% confidence interval (CI) 0.86-1.79] and lower for Parkinson disease (IRR 0.81, 95% CI 0.67-0.97) among workers exposed to ≥0.1 μT compared with the Danish population. For the highest level of exposure (≥1.0 μT), IRRs of 1.44, 1.78, 1.40 and 1.34 were observed for dementia, motor neurone disease, multiple sclerosis and epilepsy, respectively. CONCLUSIONS: We observed elevated risks of dementia, motor neurone disease, multiple sclerosis and epilepsy and lower risks of Parkinson disease in relation to exposure to ELF-MF in a large cohort of utility employees.

(E) Pelletier SJ, Lagacé M, St-Amour I, Arsenault D, Cisbani G, Chabrat A, Fecteau S, Lévesque M, Cicchetti F. The morphological and molecular changes of brain cells exposed to direct current electric field stimulation. Int J Neuropsychopharmacol. 18:pyu090, 2014 (CE, AE,MC, CC, EF)

BACKGROUND: The application of low-intensity direct current electric fields (DCEFs) has been experimentally used in the clinic to treat a number of brain disorders. predominantly using transcranial direct current stimulation (tDCS) approaches. However, the cellular and molecular changes induced by such treatment remain largely unknown. METHODS: Here, we tested various intensities of DCEFs (0, 25, 50 and 100 V/m) in a well-controlled in vitro environment in order to investigate the responses of neurons, microglia and astrocytes to this type of stimulation. This included morphological assessments of the cells, viability as well as shape and fiber outgrowth relative to the orientation of the DCEF. We also undertook ELISA assays and western immunoblotting to identify which molecular pathways were affected by DCEFs. RESULTS: In response to DCEF, neurons developed an elongated cell body shape with neurite outgrowth that was associated with a significant increase in GAP-43. Fetal midbrain dopaminergic explants grown in a collagen gel matrix also showed a reorientation of their neurites towards the cathode. BV2 microglial cells adopted distinct morphological changes with an increase in COX-2 expression but these were dependent on whether they had already been activated with lipopolysaccharide (LPS). Finally, astrocytes displayed elongated cell bodies with cellular filopodia that were oriented perpendicular to the DCEF. CONCLUSION: we show that cells of the central nervous system can respond to DCEFs both in terms of their morphological shape and molecular expression of certain proteins and this in turn can help us to begin understand the mechanisms underlying the clinical benefits of DCEF.

(NE) Percherancier Y, Goudeau B, Charlet de Sauvage R, de Gannes FP, Haro E, Hurtier A, Sojic N, Lagroye I, Arbault S, Veyret B. Effects of 50 Hz magnetic fields on gap

junctional intercellular communication in NIH3T3 cells. Bioelectromagnetics. 36:287-293, 2015. (CS, AE, FC)

The present study focused on gap junctional intercellular communication (GJIC) as a target for biological effects of extremely low-frequency (ELF) magnetic field (MF) exposure. Fluorescence recovery after photobleaching microscopy (FRAP) was used to visualize diffusion of a fluorescent dye between NIH3T3 fibroblasts through gap junctions. The direct effect of 24 h exposure to 50 Hz MF at 0.4 or 1 mT on GJIC function was assessed in one series of experiments. The potential synergism of MF with an inhibitor of GJIC, phorbol ester (TPA), was studied in another series by observing FRAP when NIH3T3 cells were incubated with TPA for 1 h following 24 h exposure to MF. In contrast to other reports of ELF-MF effects on GJIC, under our experimental conditions we observed neither direct inhibition of GJIC nor synergism with TPA-induced inhibition from 50 Hz MF exposures.

(E) Perentos N, Croft RJ, McKenzie RJ, Cvetkovic D, Cosic I. The effect of GSM-like ELF radiation on the alpha band of the human resting EEG. Conf Proc IEEE Eng Med Biol Soc. 2008:5680-5683, 2008. (HU, EE)

Mobile phone handsets such as those operating in the GSM network emit extremely low frequency electromagnetic fields ranging from DC to at least 40 kHz. As a subpart of an extended protocol, the influence of these fields on the human resting EEG has been investigated in a fully counter balanced, double blind, cross-over design study that recruited 72 healthy volunteers. A decrease in the alpha frequency band was observed during the 20 minutes of ELF exposure in the exposed hemisphere only. This result suggests that ELF fields as emitted from GSM handsets during the DTX mode may have an effect on the resting alpha band of the human EEG.

(E) Piacentini R, Ripoli C, Mezzogori D, Azzena GB, Grassi C. Extremely low-frequency electromagnetic fields promote in vitro neurogenesis via upregulation of Ca(v)1-channel activity. J Cell Physiol. 215(1):129-139, 2008. (CS, AE, MC, MA)

We previously reported that exposure to extremely low-frequency electromagnetic fields (ELFEFs) increases the expression and function of voltage-gated Ca2+)channels and that Ca2+ influx through Ca(v)1 channels plays a key role in promoting the neuronal differentiation of neural stem/progenitor cells (NSCs). The present study was conducted to determine whether ELFEFs influence the neuronal differentiation of NSCs isolated from the brain cortices of newborn mice by modulating Ca(v)1-channel function. In cultures of differentiating NSCs exposed to ELFEFs (1 mT, 50 Hz), the percentage of cells displaying immunoreactivity for neuronal markers (beta-III-tubulin, MAP2) and for Ca(v)1.2 and Ca(v)1.3 channels was markedly increased. NSC-differentiated neurons in ELFEF-exposed cultures also exhibited significant increases in spontaneous firing, in the percentage of cells exhibiting Ca2+ transients in response to KCl stimulation, in the amplitude of these transients and of Ca2+ currents generated by the activation of Ca(v)1 channels. When the Ca(v)1-channel blocker nifedipine (5 microM) was added to the culture medium, the neuronal yield of NSC differentiation dropped significantly, and ELFEF exposure no longer produced significant increases in beta-III-tubulin- and MAP2-

immunoreactivity rates. In contrast, the effects of ELFEFs were preserved when NSCs were cultured in the presence of either glutamate receptor antagonists or Ca(v)2.1- and Ca(v)2.2-channel blockers. ELFEF stimulation during the first 24 h of differentiation caused Ca(v)1-dependent increases in the number of cells displaying CREB phosphorylation. Our data suggest that ELFEF exposure promotes neuronal differentiation of NSCs by upregulating Ca(v)1-channel expression and function.

(E) Pietramala K, Greco A, Garoli A, Roblin D. Effects of Extremely Low-Frequency Electromagnetic Field Treatment on ASD Symptoms in Children: A Pilot Study. Brain Sci 14(12):1293, 2024. (HU, CE, BE, MA)

Background/objectives: Autism Spectrum Disorder (ASD) are neurodevelopmental disorders marked by challenges in social interaction, communication, and repetitive behaviors. People with ASD may exhibit repetitive behaviors, unique ways of learning, and different ways of interacting with the world. The term "spectrum" reflects the wide variability in how ASD manifests in individuals, including differences in abilities, symptoms, and support needs, and conditions characterized by difficulties in social interactions, communication, restricted interests, and repetitive behaviors. Inflammation plays a crucial role in the pathophysiology, with increased pro-inflammatory cytokines in cerebrospinal fluid. Previous studies with transcranial magnetic stimulation have shown promising results, suggesting nervous system susceptibility to electromagnetic fields, with evidence indicating that extremely low-frequency electromagnetic field (ELF-EMF) treatment may modulate inflammatory responses through multiple pathways, including the reduction of pro-inflammatory cytokines like IL-6 and TNF-α, and the enhancement of anti-inflammatory mediators. **Methods:** This pilot study included 20 children (ages 2-13) with a confirmed diagnosis of ASD. A 15-week protocol involved ELF-EMF treatments using the SEQEX device, with specific day and night programs. Assessment was conducted through standardized pre- and post-treatment tests: Achenbach Child Behavior Checklist, Peabody Picture Vocabulary Test-4, Expressive One Word Picture Vocabulary Test-4, and Conner's 3GI. **Results:** Statistically significant improvements were observed in receptive language (PPVT-4: from 74.07 to 90.40, $p = 0.002$) and expressive language (EOWPVT-4: from 84.17 to 90.50, $p = 0.041$). Notable reductions, with statistical significance, were found in externalizing problems across both age groups (1.5-5 years: $p = 0.028$; 6-18 years: $p = 0.027$), with particular improvement in attention and behavioral problems. The results were observed over a short period of 15 weeks, therefore excluding the possibility of coincidental age-related gains, that would typically occur during a normal developmental timeframe. Parent evaluations showed significant reduction in ASD symptoms, particularly in the 1.5-5 years group ($p = 0.046$). **Conclusions:** ELF-EMF treatment demonstrated a high safety profile and efficacy in mitigating ASD-related symptoms. The observed improvements suggest both direct effects on central and autonomic nervous systems and indirect effects through inflammatory response modulation. Further studies are needed to confirm these promising results through broader demographics and randomized control designs.

(E) Podda MV, Leone L, Barbati SA, Mastrodonato A, Li Puma DD, Piacentini R, Grassi C. Extremely low-frequency electromagnetic fields enhance the survival of newborn neurons in the mouse hippocampus. Eur J Neurosci. 39:893-903, 2014. (AS, CS, CE, AE, BE, CC, MA)

In recent years, much effort has been devoted to identifying stimuli capable of enhancing adult neurogenesis, a process that generates new neurons throughout life, and that appears to be dysfunctional in the senescent brain and in several neuropsychiatric and neurodegenerative diseases. We previously reported that in vivo exposure to extremely low-frequency electromagnetic fields (ELFEFs) promotes the proliferation and neuronal differentiation of hippocampal neural stem cells (NSCs) that functionally integrate in the dentate gyrus. Here, we extended our studies to specifically assess the influence of ELFEFs on hippocampal newborn cell survival, which is a very critical issue in adult neurogenesis regulation. Mice were injected with 5-bromo-2'-deoxyuridine (BrdU) to label newborn cells, and were exposed to ELFEFs 9 days later, when the most dramatic decrease in the number of newly generated neurons occurs. The results showed that ELFEF exposure (3.5 h/day for 6 days) enhanced newborn neuron survival as documented by double staining for BrdU and doublecortin, to identify immature neurons, or NeuN labeling of mature neurons. The effects of ELFEFs were associated with enhanced spatial learning and memory. In an in vitro model of hippocampal NSCs, ELFEFs exerted their pro-survival action by rescuing differentiating neurons from apoptotic cell death. Western immunoblot assay revealed reduced expression of the pro-apoptotic protein Bax, and increased levels of the anti-apoptotic protein Bcl-2, in the hippocampi of ELFEF-exposed mice as well as in ELFEF-exposed NSC cultures, as compared with their sham-exposed counterparts. Our results may have clinical implications for the treatment of impaired neurogenesis associated with brain aging and neurodegenerative diseases.

(NE) Poulletier de Gannes F, Ruffié G, Taxile M, Ladevèze E, Hurtier A, Haro E, Duleu S, Charlet de Sauvage R, Billaudel B, Geffard M, Veyret B, Lagroye I. Amyotrophic lateral sclerosis (ALS) and extremely-low frequency (ELF) magnetic fields: a study in the SOD-1 transgenic mouse model. Amyotroph Lateral Scler. 10(5-6):370-373, 2009.(AS, CE, FC)

There is some evidence from epidemiological studies of an association between occupational exposure to electromagnetic fields and Amyotrophic Lateral Sclerosis (ALS). Our aim was to perform, for the first time, an animal study in a controlled magnetic environment. We used the SOD-1 mouse model to assess the possible effect of ELF magnetic fields on development of the disease. Seven mice per group were exposed to 50 Hz magnetic fields at two intensities (100 and 1000 microT(rms)) before the onset of the clinical signs of ALS. Exposure lasted 7 weeks, and body weight, motor performance and life span were monitored. Our results did not reveal any evidence of a link between ELF exposure and ALS in this transgenic animal model.

(E) Prasad A, Teh DBL, Blasiak A, Chai C, Wu Y, Gharibani PM, Yang IH, Phan TT, Lim KL, Yang H, Liu X, All AH. Static Magnetic Field Stimulation Enhances Oligodendrocyte Differentiation and Secretion of Neurotrophic Factors. Sci Rep. 7(1):6743, 2017. (CS, CE, CC, FC)

The cellular-level effects of low/high frequency oscillating magnetic field on excitable cells such as neurons are well established. In contrast, the effects of a homogeneous,

static magnetic field (SMF) on Central Nervous System (CNS) glial cells are less investigated. Here, we have developed an in vitro SMF stimulation set-up to investigate the genomic effects of SMF exposure on oligodendrocyte differentiation and neurotrophic factors secretion. Human oligodendrocytes precursor cells (OPCs) were stimulated with moderate intensity SMF (0.3 T) for a period of two weeks (two hours/day). The differential gene expression of cell activity marker (c-fos), early OPC (Olig1, Olig2. Sox10), and mature oligodendrocyte markers (CNP, MBP) were quantified. The enhanced myelination capacity of the SMF stimulated oligodendrocytes was validated in a dorsal root ganglion microfluidics chamber platform. Additionally, the effects of SMF on the gene expression and secretion of neurotrophic factors- BDNF and NT3 was quantified. We also report that SMF stimulation increases the intracellular calcium influx in OPCs as well as the gene expression of L-type channel subunits- CaV1.2 and CaV1.3. Our findings emphasize the ability of glial cells such as OPCs to positively respond to moderate intensity SMF stimulation by exhibiting enhanced differentiation, functionality as well as neurotrophic factor release.

(E) Rabey JM, Dobronevsky E, Aichenbaum S, Gonen O, Marton RG, Khaigrekht M. Repetitive transcranial magnetic stimulation combined with cognitive training is a safe and effective modality for the treatment of Alzheimer's disease: a randomized, double-blind study. J Neural Transm (Vienna). 120(5):813-819, 2013. (HU, CE, BE, FC, MA, ND)

Cortical excitability can be modulated using repetitive transcranial magnetic stimulation (rTMS). Previously, we showed that rTMS combined with cognitive training (rTMS-COG) has positive results in Alzheimer's disease (AD). The goal of this randomized double-blind, controlled study was to examine the safety and efficacy of rTMS-COG in AD. Fifteen AD patients received 1-h daily rTMS-COG or sham treatment (seven treated, eight placebo), five sessions/week for 6 weeks, followed by biweekly sessions for 3 months. The primary outcome was improvement of the cognitive score. The secondary outcome included improvement in the Clinical Global Impression of Change (CGIC) and Neuropsychiatric Inventory (NPI). There was an improvement in the average ADAS-cog score of 3.76 points after 6 weeks in the treatment group compared to 0.47 in the placebo group and 3.52 points after 4.5 months of treatment, compared to worsening of 0.38 in the placebo (P = 0.04 and P = 0.05, respectively). There was also an improvement in the average CGIC score of 3.57 (after 6 weeks) and 3.67 points (after 4.5 months), compared to 4.25 and 4.29 in the placebo group (mild worsening) (P = 0.05 and P = 0.05, respectively). NPI improved non-significantly. In summary, the NeuroAD system offers a novel, safe and effective therapy for improving cognitive function in AD.

(E) Rauš S, Selaković V, Manojlović-Stojanoski M, Radenović L, Prolić Z, Janać B. Response of Hippocampal Neurons and Glial Cells to Alternating Magnetic Field in Gerbils Submitted to Global Cerebral Ischemia. Neurotox Res. 23(1):79-91, 2013. (AS, CE, MC, MA)

The purpose of this study was to determine whether exposure to an extremely low-frequency magnetic field (ELF-MF, 50 Hz) affects the outcome of postischemic damage in the

hippocampus of Mongolian gerbils. After 10-min bilateral carotid occlusion, the gerbils were continuously exposed to ELF-MF (average magnetic induction at the center of the cage was 0.5 mT) for 7 days. The impact of ELF-MF was estimated immediately (the 7th day after reperfusion) and 7 days after cessation of exposure (the 14th day after reperfusion) compared with ischemic gerbils without ELF-MF exposure. Applying stereological methods, histological evaluation of changes in the hippocampus was done for determining its volume, volume densities of degenerating neurons and astrocytes, as well as the number of microglial cells per unit area. ELF-MF per se did not induce any morphological changes, while 10-min global cerebral ischemia led to neuronal death, especially in CA1 region of the hippocampus, as expected. Ischemic gerbils exposed to ELF-MF had significantly a lower degree of cell loss in the examined structure and greater responses of astrocytes and microglial cells than postischemic gerbils without exposure on the seventh day after reperfusion (immediate effect of ELF-MF). Similar response was observed on the 14th day after reperfusion (delayed effect of ELF-MF); however, differences in measured parameters were low and insignificant. Applied ELF-MF has possible neuroprotective function in the hippocampus, as the most sensitive brain structure in the model of global cerebral ischemia, through reduction of neuronal death and activation of astrocytes and microglial cells.

(E) Rauš S, Selaković V, Radenović L, Prolić Z, Janać B. Extremely low frequency magnetic field induced changes in motor behaviour of gerbils submitted to global cerebral ischemia. Behav Brain Res. 228(2):241-246, 2012. (AS, CE, BE, MA)

The purpose of this study was to evaluate behavioural effects of an extremely low frequency magnetic field (ELF-MF) in 3-month-old Mongolian gerbils submitted to global cerebral ischemia. After 10-min occlusion of both common carotid arteries, the gerbils were placed in the vicinity of an electromagnet and continuously exposed to ELF-MF (50Hz, 0.5mT) for 7 days. Their behaviour (locomotion, stereotypy, rotations, and immobility) was monitored on days 1, 2, 4, 7, and 14 after reperfusion for 60 min in the open field. It was shown that the 10-min global cerebral ischemia per se induced a significant motor activity increase (locomotion, stereotypy and rotations), and consequently immobility decrease until day 4 after reperfusion, compared to control gerbils. Exposure to ELF-MF inhibited development of ischemia-induced motor hyperactivity during the whole period of registration, but significantly in the first 2 days after reperfusion, when the postischemic hyperactivity was most evident. Motor activity of these gerbils was still significantly increased compared to control ones, but only on day 1 after reperfusion. Our results revealed that the applied ELF-MF (50Hz, 0.5mT) decreased motor hyperactivity induced by the 10-min global cerebral ischemia, via modulation of the processes that underlie this behavioural response.

(E) Rauš Balind S, Selaković V, Radenović L, Prolić Z, Janać B.Extremely Low Frequency Magnetic Field (50 Hz, 0.5 mT) Reduces Oxidative Stress in the Brain of Gerbils Submitted to Global Cerebral Ischemia. PLoS One. 9(2):e88921, 2014. (AS, CE, OX, CC, MA)

Magnetic field as ecological factor has influence on all living beings. The aim of this study was to determine if extremely low frequency magnetic field (ELF-MF, 50 Hz, 0.5 mT) affects oxidative

stress in the brain of gerbils submitted to 10-min global cerebral ischemia. After occlusion of both carotid arteries, 3-month-old gerbils were continuously exposed to ELF-MF for 7 days. Nitric oxide and superoxide anion production, superoxide dismutase activity and index of lipid peroxidation were examined in the forebrain cortex, striatum and hippocampus on the 7(th) (immediate effect of ELF-MF) and 14(th) day after reperfusion (delayed effect of ELF-MF). Ischemia per se increased oxidative stress in the brain on the 7(th) and 14(th) day after reperfusion. ELF-MF also increased oxidative stress, but to a greater extent than ischemia, only immediately after cessation of exposure. Ischemic gerbils exposed to ELF-MF had increased oxidative stress parameters on the 7(th) day after reperfusion, but to a lesser extent than ischemic or ELF-MF-exposed animals. On the 14(th) day after reperfusion, oxidative stress parameters in the brain of these gerbils were mostly at the control levels. Applied ELF-MF decreases oxidative stress induced by global cerebral ischemia and thereby reduces possible negative consequences which free radical species could have in the brain. The results presented here indicate a beneficial effect of ELF-MF (50 Hz, 0.5 mT) in the model of global cerebral ischemia.

(E) Rauš Balind S, M. Manojlović-Stojanoski, V. Milošević, D. Todorović, L. Nikolić, B. Petković. Short- and long-term exposure to alternating magnetic field (50 Hz, 0.5 mT) affects rat pituitary ACTH cells: Stereological study. Environ Toxicol 31(4):461-468, 2016. (AS, CE, MC)

The aim of the present study was to determine does extremely low frequency magnetic field (ELF-MF, 50 Hz, 0.5 mT) affect pituitary adrenocorticotroph (ACTH) cells in adult animals. We performed two series of experiments: (1) short-term exposure of 3-month-old rats to ELF-MF for 1 and 7 days, and (2) long-term exposure of rats to ELF-MF from their conception to 3 months of age. Stereological study was performed on immunolabeled pituitary ACTH cells. The total number and volume of ACTH cells, the volume of their nuclei and pituitary volume were measured. ELF-MF exposure for 1 day significantly decreased total number and volume of ACTH cells, the volume of their nuclei, as well as pituitary volume. ELF-MF exposure for 7 days significantly reduced only the volume of ACTH cells. Life-long exposure to ELF-MF induced decrease in the volume of ACTH cells and pituitary volume. We can conclude that the applied ELF-MF has a strong influence on morphometrical parameters of the pituitary ACTH cells and could be considered as a stressogenic factor.

(E) Ravera S, Bianco B, Cugnoli C, Panfoli I, Calzia D, Morelli A, Pepe IM. Sinusoidal ELF magnetic fields affect acetylcholinesterase activity in cerebellum synaptosomal membranes. Bioelectromagnetics. 31(4):270-276, 2010. (CS, AE, CE)

The effects of extremely low frequency magnetic fields (ELF-MF) on acetylcholinesterase (AChE) activity of synaptosomal membranes were investigated. Sinusoidal fields with 50 Hz frequency and different amplitudes caused AChE activity to decrease about 27% with a threshold of about 0.74 mT. The decrease in enzymatic activity was independent of the time of permanence in the field and was completely reversible. Identical results were obtained with exposure to static MF of the same amplitudes. Moreover, the inhibitory effects on enzymatic activity are spread over frequency windows with different maximal values at 60, 200, 350, and 475 Hz. When

synaptosomal membranes were solubilized with Triton, ELF-MF did not affect AChE activity, suggesting the crucial role of the membrane, as well as the lipid linkage of the enzyme, in determining the conditions for inactivation. The results are discussed in order to give an interpretation at molecular level of the macroscopic effects produced by ELF-MF on biological systems, in particular the alterations of embryo development in many organisms due to acetylcholine accumulation.

(E) Rageh MM, El-Gebaly RH, El-Bialy NS. Assessment of genotoxic and cytotoxic hazards in brain and bone marrow cells of newborn rats exposed to extremely low-frequency magnetic field. J Biomed Biotechnol. 2012:716023, 2012. (AS, CE, OX, DE)

The present study aimed to evaluate the association between whole body exposure to extremely low frequency magnetic field (ELF-MF) and genotoxic , cytotoxic hazards in brain and bone marrow cells of newborn rats. Newborn rats (10 days after delivery) were exposed continuously to 50 Hz, 0.5 mT for 30 days. The control group was treated as the exposed one with the sole difference that the rats were not exposed to magnetic field. Comet assay was used to quantify the level of DNA damage in isolated brain cells. Also bone marrow cells were flushed out to assess micronucleus induction and mitotic index. Spectrophotometric methods were used to measure the level of malondialdehyde (MDA) and the activity of glutathione (GSH) and superoxide dismutase (SOD). The results showed a significant increase in the mean tail moment indicating DNA damage in exposed group ($P < 0.01, 0.001, 0.0001$). Moreover ELF-MF exposure induced a significant ($P < 0.01, 0.001$) four folds increase in the induction of micronucleus and about three folds increase in mitotic index ($P < 0.0001$). Additionally newborn rats exposed to ELF-MF showed significant higher levels of MDA and SOD ($P < 0.05$). Meanwhile ELF-MF failed to alter the activity of GSH. In conclusion, the present study suggests an association between DNA damage and ELF-MF exposure in newborn rats.

(E) Reale M, Kamal MA, Patruno A, Costantini E, D'Angelo C, Pesce M, Greig NH. Neuronal Cellular Responses to Extremely Low Frequency Electromagnetic Field Exposure: Implications Regarding Oxidative Stress and Neurodegeneration. PLoS One. 9(8):e104973, 2014. (CS, AE, OX, ND)

Neurodegenerative diseases comprise both hereditary and sporadic conditions characterized by an identifying progressive nervous system dysfunction and distinctive neuopathophysiology. The majority are of non-familial etiology and hence environmental factors and lifestyle play key roles in their pathogenesis. The extensive use of and ever increasing worldwide demand for electricity has stimulated societal and scientific interest on the environmental exposure to low frequency electromagnetic fields (EMFs) on human health. Epidemiological studies suggest a positive association between 50/60-Hz power transmission fields and leukemia or lymphoma development. Consequent to the association between EMFs and induction of oxidative stress, concerns relating to development of neurodegenerative diseases, such as Alzheimer disease (AD), have been voiced as the brain consumes the greatest fraction of oxygen and is particularly vulnerable to oxidative stress. Exposure to extremely low frequency (ELF)-EMFs are reported to alter animal behavior and modulate biological variables, including gene expression, regulation

of cell survival, promotion of cellular differentiation, and changes in cerebral blood flow in aged AD transgenic mice. Alterations in inflammatory responses have also been reported, but how these actions impact human health remains unknown. We hence evaluated the effects of an electromagnetic wave (magnetic field intensity 1mT; frequency, 50-Hz) on a well-characterized immortalized neuronal cell model, human SH-SY5Y cells. ELF-EMF exposure elevated the expession of NOS and O2-, which were countered by compensatory changes in antioxidant catylase (CAT) activity and enzymatic kinetic parameters related to CYP-450 and CAT activity. Actions of ELF-EMFs on cytokine gene expression were additionally evaluated and found rapidly modified. Confronted with co-exposure to H2O2-induced oxidative stress, ELF-EMF proved not as well counteracted and resulted in a decline in CAT activity and a rise in O2- levels. Together these studies support the further evaluation of ELF-EMF exposure in cellular and in vivo preclinical models to define mechanisms potentially impacted in humans.

(NE) Reale M, D'Angelo C, Costantini E, Tata AM, Regen F, Hellmann-Regen J. Effect of Environmental Extremely Low-Frequency Electromagnetic Fields Exposure on Inflammatory Mediators and Serotonin Metabolism in a Human Neuroblastoma Cell Line. CNS Neurol Disord Drug Targets. 15(10):1203-1215, 2016. (CS, AE, CC)

Exposure to environmental extremely low-frequency electromagnetic fields (ELF-EMF) in everyday life is increasing and it is a matter of great debate whether exposure to ELF-EMF can be harmful to human health. The neuropathology and symptoms of neurodegenerative disease depends on factors other than genetic predispositions, such as environmental exposure to disease-related risk factors. Research focusing on a possible contribution of ELF-EMF to cell injury and to the development of neurodegenerative disorders is characterized by conflicting data from epidemiological and animal studies. Due to lack of a direct link between neurodegenerative processes and ELF-EMF exposure, our goal was to investigate if ELF-EMF exposure may represent a possible risk factor. In the present study, using neuronal-like SH-SY5Y neuroblastoma cells, we show that the balance between generation and elimination of reactive oxygen species, as well as the balance between pro- and anti-inflammatory cytokines linked to oxidative stress, was maintained ensuring that cells respond properly to ELF-EMF (50Hz /1mT). In SH-SY5Y-exposed cells we observed increased intracellular 5-hydroxyindoleacetic acid/5-hydroxytryptamine ratio reflecting the rate of transmitter synthesis, catabolism and release, while matrix metalloproteinases that play critical roles in neuronal cell death were not significantly altered. The results presented here indicate that changes caused by short (1h-3h) and sub-chronic (48 h) exposure to 50Hz/1mT ELF-EMF in SH-SY5Y cells are minor in comparison to the neuronal cell damage expected to underlie neurodegeneration or cognitive impairment. Thus, these results are in accord with epidemiological studies that have provided little support for a link between ELF-EMFs and neurodegeneration.

(E) Renáta Szemerszky R, D. Zelena, I. Barna, G. Bárdos. Stress-related endocrinological and psychopathological effects of short- and long-term 50Hz electromagnetic field exposure in rats. Brain Res Bull 81(1):92-99, 2010. (VO, LE, GE)

It is believed that different electromagnetic fields do have beneficial and harmful biological effects. The aim of the present work was to study the long-term consequences of 50 Hz electromagnetic field (ELF-EMF) exposure with special focus on the development of chronic stress and stress-induced psychopathology. Adult male Sprague-Dawley rats were exposed to ELF-EMF (50 Hz, 0.5 mT) for 5 days, 8h daily (short) or for 4-6 weeks, 24h daily (long). Anxiety was studied in elevated plus maze test, whereas depression-like behavior of the long-treated group was examined in the forced swim test. Some days after behavioral examination, the animals were decapitated among resting conditions and organ weights, blood hormone levels as well as proopiomelanocortin mRNA level from the anterior lobe of the pituitary gland were measured. Both treatments were ineffective on somatic parameters, namely none of the changes characteristic to chronic stress (body weight reduction, thymus involution and adrenal gland hypertrophy) were present. An enhanced blood glucose level was found after prolonged ELF-EMF exposure ($p=0.013$). The hormonal stress reaction was similar in control and short-term exposed rats, but significant proopiomelanocortin elevation ($p<0.000$) and depressive-like behavior (enhanced floating time; $p=0.006$) were found following long-term ELF-EMF exposure. Taken together, long and continuous exposure to relatively high intensity electromagnetic field may count as a mild stress situation and could be a factor in the development of depressive state or metabolic disturbances. Although we should stress that the average intensity of the human exposure is normally much smaller than in the present experiment.

Ritz T, Adem S, Schulten K. A model for photoreceptor-based magnetoreception in birds. Biophys J. 78(2):707-718, 2000. (Review)

A large variety of animals has the ability to sense the geomagnetic field and utilize it as a source of directional (compass) information. It is not known by which biophysical mechanism this magnetoreception is achieved. We investigate the possibility that magnetoreception involves radical-pair processes that are governed by anisotropic hyperfine coupling between (unpaired) electron and nuclear spins. We will show theoretically that fields of geomagnetic field strength and weaker can produce significantly different reaction yields for different alignments of the radical pairs with the magnetic field. As a model for a magnetic sensory organ we propose a system of radical pairs being 1) orientationally ordered in a molecular substrate and 2) exhibiting changes in the reaction yields that affect the visual transduction pathway. We evaluate three-dimensional visual modulation patterns that can arise from the influence of the geomagnetic field on radical-pair systems. The variations of these patterns with orientation and field strength can furnish the magnetic compass ability of birds with the same characteristics as observed in behavioral experiments. We propose that the recently discovered photoreceptor cryptochrome is part of the magnetoreception system and suggest further studies to prove or disprove this hypothesis.

(E) Reyes-Guerrero G, Guzmán C, García DE, Camacho-Arroyo I, Vázquez-García M. Extremely low-frequency electromagnetic fields differentially regulate estrogen receptor-alpha and -beta expression in the rat olfactory bulb. Neurosci Lett. 471(2):109-13, 2010. (AS, AE, CC)

Recently, the effects of extremely low-frequency electromagnetic fields (ELF EMF) on biological systems have been extensively investigated. In this report, the influence of ELF EMF on olfactory bulb (OB) estrogen receptor-alpha (ER alpha) mRNA and -beta (ER beta) mRNA expression was studied by RT-PCR in adult female and male rats. Results reveal for the first time that ELF EMF exerted a biphasic effect on female OB ER beta mRNA gene expression, which increased during diestrous and decreased during estrous. We did not observe any influence of ELF EMF on female OB ER alpha mRNA expression. Our data demonstrate a fluctuating pattern of ER-alpha and -beta mRNA expression in the female OB throughout the phases of the estrous cycle in non-ELF EMF-exposed animals. Thus the highest ER alpha expression was observed in diestrous and the lowest in proestrous. The pattern of ER beta mRNA was less variable, the lowest expression was observed in diestrous. ER-alpha mRNA and -beta mRNA expression level in the male OB did not exhibit any variation either in ELF EMF-exposed or non-ELF EMF-exposed animals. In summary, ELF EMF modulate ER beta gene expression in the OB of female adult rats but not in males.

(E) Rivadulla C, Aguilar J, Coletti M, Aguila J, Prieto S, Cudeiro J. Static magnetic fields reduce epileptiform activity in anesthetized rat and monkey. Sci Rep 8(1):15985, 2018.(AS, AE, EE, MA)

Increasing evidence indicates that static magnetic fields (SMF) reduce cortical activity in both human and animal models. The aim of this work was to investigate the effect of SMF on epileptiform cortical activity, a condition related to an abnormal increase in neuronal excitability. The first experimental block included a Pilocarpine rat model of epilepsy, in which a magnetic neodymium nickel-plated cylinder, a magnetic field of 0.5 T, or "sham" were placed over the skull. In the second experimental block, we recorded epileptic-like activity in the visual cortex of a monkey (Macaca mulatta) under control conditions and in the presence of the magnet. Between 15 and 30 minutes after the second dose of Pilocarpine, EEG changes compatible with seizure like events induced by Pilocarpine were clearly observed in the control animals (sham stimulation). Similar effects were visible in the animals exposed to the real magnet after 1-2 hours. In the monkey, SMF over the cortical focus clearly reduced abnormal activity: the intensity threshold for visual induction increased and the severity and duration decreased. These results reinforce the view that static magnets modulate cortical activity and open the door to the future therapeutic use of SMF in epilepsy as a complement to current pharmacological treatments

(E) Ross ML, Koren SA, Persinger MA. Physiologically patterned weak magnetic fields applied over left frontal lobe increase acceptance of false statements as true. Electromagn Biol Med. 27(4):365-371, 2008. (HU, AE, BE)

Fifty men and women were exposed to only one of four experimentally generated magnetic fields over the left prefrontal region (above the eyebrow) or to a sham field immediately after the words "true" or "false" were presented following statements of definitions of words for a "foreign language". Three of the patterns (25 Hz, 50 Hz, or burst-firing) with intensities between 1 and 10 microT were presented for 1 s during the refutation process (immediately after the offset of "true" or "false") for specific statements from a total of 28 statements. The fourth pattern was a variable approximately 7-10 Hz (10 nT) field generated from the circuitry that was present continuously during the entire experiment. When the statements were presented

again, the groups who had received the burst-firing ("limbic") or 25 Hz pulsed magnetic fields during the refutation process accepted about twice the number of false statements as true compared to those exposed to the 50 Hz field or sham-field conditions. The treatments did not significantly affect the numbers of true statements accepted as false. These results suggest that the appropriately pulsed magnetic field during the refutation process of what one has been told or has heard can increase the probability a person will accept a false statement as true.

(E) Ross CL, Teli T, Harrison BS. Effect of electromagnetic field on cyclic adenosine monophosphate (cAMP) in a human mu-opioid receptor cell model. Electromagn Biol Med. 35:206-213, 2016. (CS, AE, CC, MA)

During the cell communication process, endogenous and exogenous signaling affect normal as well as pathological developmental conditions. Exogenous influences such as extra-low-frequency electromagnetic field (EMF) have been shown to effect pain and inflammation by modulating G-protein receptors, down-regulating cyclooxygenase-2 activity, and affecting the calcium/calmodulin/nitric oxide pathway. Investigators have reported changes in opioid receptors and second messengers, such as cyclic adenosine monophosphate (cAMP), in opiate tolerance and dependence by showing how repeated exposure to morphine decreases adenylate cyclase activity causing cAMP to return to control levels in the tolerant state, and increase above control levels during withdrawal. Resonance responses to biological systems using exogenous EMF signals suggest that frequency response characteristics of the target can determine the EMF biological response. In our past research we found significant down regulation of inflammatory markers tumor necrosis factor alpha (TNF-α) and nuclear factor kappa B (NFκB) using 5 Hz EMF frequency. In this study cAMP was stimulated in Chinese Hamster Ovary (CHO) cells transfected with human mu-opioid receptors, then exposed to 5 Hz EMF, and outcomes were compared with morphine treatment. Results showed a 23% greater inhibition of cAMP-treating cells with EMF than with morphine. In order to test our results for frequency specific effects, we ran identical experiments using 13 Hz EMF, which produced results similar to controls. This study suggests the use of EMF as a complementary or alternative treatment to morphine that could both reduce pain and enhance patient quality of life without the side-effects of opiates.

(E) Rostami A, Shahani M, Zarrindast MR, Semnanian S, Rahmati Roudsari M, Rezaei Tavirani M, Hasanzadeh H. Effects of 3 Hz and 60 Hz Extremely Low Frequency Electromagnetic Fields on Anxiety-Like Behaviors, Memory Retention of Passive Avoidance and Electrophysiological Properties of Male Rats. J Lasers Med Sci. 7(2):120-125, 2016. (AS, CE, BE, EE, CC)

INTRODUCTION: The effects of electromagnetic fields on biological organisms have been a controversial and also interesting debate over the past few decades, despite the wide range of investigations, many aspects of extremely low frequency electromagnetic fields (ELF/EMFs) effects including mechanism of their interaction with live organisms and also their possible biological applications still remain ambiguous. In the present study, we investigated whether the exposures of ELF/EMF with frequencies of 3 Hz and 60 Hz can affect the memory, anxiety like behaviors, electrophysiological properties and brain's proteome in rats. **METHODS:** Male rats were exposed to 3 Hz and 60 Hz ELF/EMFs in a protocol consisting of 2 cycles of 2 h/day exposure for 4 days separated with a 2-day interval. Short term memory and anxiety like

behaviors were assessed immediately, 1 and 2 weeks after the exposures. Effects of short-term exposure were also assessed using electrophysiological approach immediately after 2 hours exposure. **RESULTS:** Behavioral test revealed that immediately after the end of exposures, locomotor activity of both 3 Hz and 60 Hz exposed groups significantly decreased compared to sham group. This exposure protocol had no effect on anxiety like behavior during the 2 weeks after the treatment and also on short term memory. A significant reduction in firing rate of locus coeruleus (LC) was found after 2 hours of both 3 Hz and 60 Hz exposures. Proteome analysis also revealed global changes in whole brain proteome after treatment. **CONCLUSION:** Here, some evidence regarding the fact that such exposures can alter locomotor activity and neurons firing rate in male rats were presented.

(E) Rusovan A, Kanje M, Mild KH. The stimulatory effect of magnetic fields on regeneration of the rat sciatic nerve is frequency dependent. Exp Neurol 117(1):81-84, 1992. (CS, AE, MC, MA)

The effects of exposure to sinusoidal magnetic fields on regeneration of the rat sciatic nerve were studied. Regeneration distances were measured after a crush lesion. The rats were exposed to a 0.1-mT magnetic field of various frequencies (50-2000 Hz) inside a pair of Helmholtz coils for various periods of time. Regeneration was measured by the pinch test or by immunocytochemical staining for neurofilaments 3, 4, or 6 days after the lesioning. Frequencies of 250, 500, and 1000 Hz significantly increased the regeneration distance. Higher (2000 Hz) and lower (50 Hz) frequencies had no effect. Maximal stimulation was obtained at 1000 Hz. At this frequency the rate of regeneration was increased by 24%. The results suggest that a broad frequency window exists within which the regeneration processes are sensitive to perturbation by magnetic fields and/or currents induced in the animal.

(E)Saha R, Goyal A, Yuen J, Oh Y, Bloom R, Benally OJ, Wu K, Netoff TI, Low WC, Bennet K, Lee KH, Shin H, Wang J-P. Micromagnetic Stimulation (µMS) Controls Dopamine Release: An in vivo Study Using WINCS Harmoni. Biomed Phys Eng Express 2025 Feb 27. doi: 10.1088/2057-1976/adbaf9. Online ahead of print. (AS, AE, CC, MA, ND)

Research into the role of neurotransmitters in regulating normal and pathologic brain functions has made significant progress. Yet, clinical trials that aim to improve therapeutic interventions do not take advantage of the in vivo changes in the neurochemistry that occur in real time during disease progression, drug interactions or response to pharmacological, cognitive, behavioral, and neuromodulation therapies. In this work, we used the WINCS Harmoni tool to study the real time in vivo changes in dopamine release in rodent brains for the micromagnetic neuromodulation therapy. Although still in its infancy, micromagnetic stimulation (µMS) using micro-meter sized coils or microcoils (µcoils) has shown incredible promise in spatially selective, galvanic contact free and highly focal neuromodulation. These µcoils are powered by a time-varying current which generates a magnetic field. As per Faraday's Laws of Electromagnetic Induction, this magnetic field induces an electric field in a conducting medium (here, the brain tissues). We used a solenoidal-shaped µcoil to stimulate the medial forebrain bundle (MFB) of the rodent brain in vivo. The evoked in vivo dopamine releases in the striatum were tracked in real time by carbon fiber microelectrodes (CFM) using fast scan cyclic voltammetry (FSCV). Our experiments report that µcoils can successfully activate the MFB in

rodent brains, triggering dopamine release in vivo. We further show that the successful release of dopamine upon micromagnetic stimulation is dependent on the orientation of the μcoil. Furthermore, varied intensities of μMS can control the concentration of dopamine releases in the striatum. This work helps us better understand the brain and its conditions arising from a new therapeutic intervention, like μMS, at the level of neurotransmitter release. Despite its early stage, this study potentially paves the path for μMS to enter the clinical world as a precisely controlled and optimized neuromodulation therapy.

(E) Sakhaie MH, Soleimani M, Pourheydar B, Majd Z, Atefimanesh P, Asl SS, Mehdizadeh M. Effects of Extremely Low-Frequency Electromagnetic Fields on Neurogenesis and Cognitive Behavior in an Experimental Model of Hippocampal Injury. Behav Neurol. 2017:9194261, 2017. (AS, CE, BE, MC, MA, ND)

Exposure to extremely low-frequency electromagnetic fields may induce constant modulation in neuronal plasticity. In recent years, tremendous efforts have been made to design a suitable strategy for enhancing adult neurogenesis, which seems to be deterred due to brain senescence and several neurodegenerative diseases. In this study, we evaluated the effects of ELF-EMF on neurogenesis and memory, following treatment with trimethyltin chloride (TMT) as a neurotoxicant. The mice in all groups (n = 56) were injected with BrdU during the experiment for seven consecutive days to label newborn cells. Spatial memory was assessed by the Morris water maze (MWM) test. By the end of the experiment, neurogenesis and neuronal differentiation were assessed in the hippocampus, using immunohistochemistry and Western blot analysis. Based on the findings, exposure to ELF-EMF enhanced spatial learning and memory in the MWM test. ELF-EMF exposure significantly enhanced the number of BrdU+ and NeuN+ cells in the dentate gyrus of adult mice ($P < 0.001$ and $P < 0.05$, resp.). Western blot analysis revealed significant upregulation of NeuroD2 in ELF-EMF-exposed mice compared to the TMT-treated group ($P < 0.05$). These findings suggest that ELF-EMF might have clinical implications for the improvement of neurodegenerative processes and could help develop a novel therapeutic approach in regenerative medicine.

(E) Sakhnini L, Al Ali H, Al Qassab N, Al Arab E, Kamal A. Subacute exposure to 50-Hz electromagnetic fields affect prenatal and neonatal mice's motor coordination. J. Appl. Phys. 111(7):07B314, 2012. (AS, CE, BE, DE)

In this study, we investigate the possible effect of ELF-EMFs on motor performance in mice (prenatal and neonatal exposed mice). The mice performance is evaluated after 5 days of subacute exposure. Immature mice have been chosen for this study because the immature rodent brain still has the capacity to undergo proliferation, differentiation, and reorganization. Results from the rotarod experiments demonstrated a pronounced deficit in the learning abilities of the prenatal exposed groups, but no pronounced effect was observed for the neonatal exposed group.

(E) Sales PM, de Andrade LM, Pitcher MR, Rola FH, Gondim FA. Levodopa enhances immobility induced by spinal cord electromagnetic stimulation in rats. Neurosci Lett. 633:196-201, 2016. (AS, CE, BE)

BACKGROUND: The repetitive ElectroMagnetic Stimulation (rEMS) is an innocuous method applied to modulate neurocircuits in real-time to study the physiology of the central nervous system and treat neuropsychiatric conditions. Preliminary data suggest that spinal rEMS induces behavioral changes in awake rats. However, the mechanisms behind this phenomenon remain largely unknown. METHODS: Twenty-five male Wistar rats were divided into five subgroups of five animals each: one subgroup was drug-free, two subgroups received Levodopa+Benserazide 250+25mg/kg for two or seven days, and the remaining two subgroups received Haloperidol 0.1 or 0.3mg/kg for two days. The animals were restrained during sham rEMS (day 1) followed by real rEMS of the cervicothoracic region at a different day (day 2 or 7, depending on subgroup). Four behavioral parameters were quantified: Walking, Climbing, Grooming, and Cornering. RESULTS: rEMS reduced Walking and increased Cornering duration when applied over the cervicothoracic region of drug-free animals. A pretreatment with Levodopa+Benserazide for two or seven days induced an additional decrease in Walking after rEMS. This reduction was maximum after the treatment for seven days and associated with extinction of Climbing and increase in Cornering. A pretreatment with Haloperidol 0.1mg/kg reduced Grooming after rEMS, but did not prevent the reduction in Walking. CONCLUSIONS: Cervicothoracic rEMS induced complex immobility responses that are in part modulated by dopaminergic pathways in rats. Further studies are necessary to determine the specific mechanisms involved.

(E) Salunke BP, Umathe SN, Chavan JG. Involvement of NMDA receptor in low-frequency magnetic field-induced anxiety in mice. Electromagn Biol Med. 33(4):312-326, 2014. (AS, CE, CC, BE)

It had been reported that exposure to extremely low-frequency magnetic field (ELFMF) induces anxiety in human and rodents. Anxiety mediates via the activation of N-methyl-d-aspartate (NMDA) receptor, whereas activation of γ-aminobutyric acid (GABA) receptor attenuates the same. Hence, the present study was carried out to understand the contribution of NMDA and/or GABA receptors modulation in ELFMF-induced anxiety for which Swiss albino mice were exposed to ELFMF (50 Hz, 10 G) by subjecting them to Helmholtz coils. The exposure was for 8 h/day for 7, 30, 60, 90 and 120 days. Anxiety level was assessed in elevated plus maze, open field test and social interaction test, on 7th, 30th, 60th, 90th and 120th exposure day, respectively. Moreover, the role of GABA and glutamate in ELFMF-induced anxiety was assessed by treating mice with muscimol [0.25 mg/kg intraperitoneally (i.p.)], bicuculline (1.0 mg/kg i.p.), NMDA (15 mg/kg i.p.) and MK-801 (0.03 mg/kg i.p.), as a $GABA_A$ and NMDA receptor agonist and antagonist, respectively. Glutamate receptor agonist exacerbated while inhibitor attenuated the ELFMF-induced anxiety. In addition, levels of GABA and glutamate were determined in regions of the brain viz, cortex, striatum, hippocampus and hypothalamus. Experiments demonstrated significant elevation of GABA and glutamate levels in the hippocampus and hypothalamus. However, GABA receptor modulators did not produce significant effect on ELFMF-induced anxiety and elevated levels of GABA at tested dose. Together, these findings suggest that ELFMF significantly induced anxiety behavior, and indicated the involvement of NMDA receptor in its effect.

(E) Salunke BP, Umathe SN, Chavan JG. Experimental evidence for involvement of nitric oxide in low frequency magnetic field induced obsessive compulsive disorder-like behavior. Pharmacol Biochem Behav. 122:273-278, 2014.

It is well documented that extremely low frequency magnetic field (ELF MF) produced effects on the function of nervous system in humans and laboratory animals. Dopaminergic and serotonergic pathways have been implicated in obsessive compulsive disorder (OCD). Recently involvement of nitric oxide (NO) in OCD-like behavior is suggested. Hence, the present study was carried out to understand the involvement of dopamine, serotonin and NO in ELF MF induced OCD-like behavior. Swiss albino mice were exposed to ELF MF (50Hz, 10G) for 8h/day for 7, 30, 60, 90 and 120days by subjecting them to Helmholtz coils. OCD-like behavior was assessed in terms of marble burying behavior (MBB) test. Results revealed that ELF MF induced time dependant MBB, on 7th, 30th, 60th, 90th, and 120th exposure day. Further, levels of dopamine, serotonin and NO after 120days of ELF MF exposure were determined in regions of the brain. The neurohumoral studies revealed that exposure to ELF MF increased NO levels in cortex, hippocampus and hypothalamus, and levels of dopamine and serotonin remain unaffected. As OCD-like behavior after ELF MF exposure was associated with higher levels of NO with no significant change in serotonin and dopamine, the effect of such exposure was studied in groups concurrently treated with NO modulators, NO precursor, L-ARG (400mg/kg) or NOS inhibitor, L-NAME (15.0mg/kg) or 7-NI (10.0mg/kg). These treatments revealed that NO precursor exacerbated and NOS inhibitors attenuated ELF MF induced OCD-like behavior with corresponding changes in the levels of NO.

(E) Samiee F, Samiee K. Effect of extremely low frequency electromagnetic field on brain histopathology of Caspian Sea Cyprinus carpio. Electromagn Biol Med. 36(1):31-38, 2017. (AS, AE, MC)

There is limited research on the effect of electromagnetic field on aquatic organisms, especially freshwater fish species. This study was conducted to evaluate the effect of extremely low frequency electromagnetic field (ELF-EMF) (50 Hz) exposure on brain histopathology of Cyprinus carpio, one of the important species of Caspian Sea with significant economic value. A total of 200 healthy fish were used in this study. They were classified randomly in two groups: sham-exposed group and experimental group, which were exposed to five different magnetic field intensities (0.1, 1, 3, 5, and 7 mT) at two different exposure times (0.5 and 1 h). Histologic results indicate that exposure of C. carpio to artificial ELF-EMF caused severe histopathological changes in the brain at field intensities ≥3 mT leading to brain necrosis. Field intensity and duration of exposure were key parameters in induction of lesion in the brain. Further studies are needed to elucidate exact mechanism of EMF exposure on the brain.

(E) Savić T, Janać B, Todorović D, Prolić Z. The embryonic and post-embryonic development in two Drosophila species exposed to the static magnetic field of 60 mT. Electromagn Biol Med. 30(2):108-114, 2011. (AS, CE, DE)

In this study, a static magnetic field influence on development and viability in two different species, Drosophila melanogaster and Drosophila hydei, was investigated. Both species completed development (egg-adult), in and out of the static magnetic field induced by double horseshoe magnet. Treated vials with eggs were placed in the gap between magnetic poles (47 mm) and exposed to the average magnetic induction of 60 mT, while control ones were kept far enough from magnetic field source. We found that exposure to the static magnetic field reduced development time in both species, but statistical significance was found only for D. hydei. Furthermore, we found that the average viability of both Drosophila species exposed to the magnetic field was significantly weaker compared to control ones. These results indicate that 60 mT static magnetic field could be considered as a potential stressor, influencing on different levels the embryonic and post-embryonic development of individuals.

(E) Schmid MR, Murbach M, Lustenberger C, Maire M, Kuster N, Achermann P, Loughran SP. Sleep EEG alterations: effects of pulsed magnetic fields versus pulse-modulated radio frequency electromagnetic fields. J Sleep Res. 21(6):620-629, 2012. (HU, AE, EE)

Studies have repeatedly shown that electroencephalographic power during sleep is enhanced in the spindle frequency range following radio frequency electromagnetic field exposures pulse-modulated with fundamental frequency components of 2, 8, 14 or 217 Hz and combinations of these. However, signals used in previous studies also had significant harmonic components above 20 Hz. The current study aimed: (i) to determine if modulation components above 20 Hz, in combination with radio frequency, are necessary to alter the electroencephalogram; and (ii) to test the demodulation hypothesis, if the same effects occur after magnetic field exposure with the same pulse sequence used in the pulse-modulated radio frequency exposure. In a randomized double-blind crossover design, 25 young healthy men were exposed at weekly intervals to three different conditions for 30 min before sleep. Cognitive tasks were also performed during exposure. The conditions were a 2-Hz pulse-modulated radio frequency field, a 2-Hz pulsed magnetic field, and sham. Radio frequency exposure increased electroencephalogram power in the spindle frequency range. Furthermore, delta and theta activity (non-rapid eye movement sleep), and alpha and delta activity (rapid eye movement sleep) were affected following both exposure conditions. No effect on sleep architecture and no clear impact of exposure on cognition was observed. These results demonstrate that both pulse-modulated radio frequency and pulsed magnetic fields affect brain physiology, and the presence of significant frequency components above 20 Hz are not fundamental for these effects to occur. Because responses were not identical for all exposures, the study does not support the hypothesis that effects of radio frequency exposure are based on demodulation of the signal only.

(E) Schneider WT, Holland RA, Keišs O, Lindecke O. Migratory bats are sensitive to magnetic inclination changes during the compass calibration period. Biol Lett 19(11):20230181, 2023. (AS, AE, BE)

The Earth's magnetic field is used as a navigational cue by many animals. For mammals, however, there are few data to show that navigation ability relies on sensing the natural magnetic

field. In night-time migrating bats, experiments demonstrating a role for the solar azimuth at sunset in the calibration of the orientation system suggest that the magnetic field is a candidate for their compass. Here, we investigated how an altered magnetic field at sunset changes the nocturnal orientation of the bat *Pipistrellus pygmaeus*. We exposed bats to either the natural magnetic field, a horizontally shifted field (120°), or the same shifted field combined with a reversal of the natural value of inclination (70° to -70°). We later released the bats and found that the take-off orientation differed among all treatments. Bats that were exposed to the 120° shift were unimodally oriented northwards in contrast to controls which exhibited a bimodal north-south distribution. Surprisingly, the orientation of bats exposed to both a 120° shift and reverse inclination was indistinguishable from a uniform distribution. These results suggest that these migratory bats calibrate the magnetic field at sunset, and for the first time, they show that bats are sensitive to the angle of magnetic inclination.

(E) Sekar S, Zhang Y, Mahabadi HM, Parvizi A, Taghibiglou C. Low-Field Magnetic Stimulation Restores Cognitive and Motor Functions in the Mouse Model of Repeated Traumatic Brain Injury: Role of Cellular Prion Protein. J Neurotrauma 36(22):3103-3114, 2019. (AS, CE, BE, CE, MA)

Traumatic brain injury (TBI)/concussion is a growing epidemic throughout the world. Memory and neurobehavioral dysfunctions are among the sequelae of TBI. Dislodgement of cellular prion protein (PrPc) and disruption of circadian rhythm have been linked to TBI. Low-field magnetic stimulation (LFMS) is a new noninvasive repetitive transcranial magnetic stimulation (rTMS) technique that generates diffused and low-intensity magnetic stimulation to deep cortical and subcortical areas. The role of LFMS on PrPc, proteins related to the circadian rhythm, and behavior alterations in a repeated TBI mouse model were studied in the present study. TBI was induced to the mice (right hemisphere) using weight-drop method, once daily for 3 days. LFMS treatment was given for 20 min once daily for 4 days (immediately after each TBI induction). The results showed that LFMS-treated TBI mice significantly improved cognitive and motor function as evidenced by open field exploration, rotarod, and novel location recognition tasks. In addition, a significant increase in PrPc and decreased glial fibrillary acidic protein levels were observed in cortical and hippocampal regions of LFMS-treated TBI mice brain compared with sham-treated TBI mice, while neuronal nuclei level was significantly increased in cortical region. In LFMS-treated mice, a decrease in proteins related to circadian rhythm were observed, compared with sham-treated TBI mice. The results obtained from the study demonstrated the neuroprotective effect of LFMS, which may be through regulating PrPc and/or proteins related to circadian rhythm. Thus, the present study suggests that LFMS may improve the subject's neurological condition following TBI.

(E) Selaković V, Rauš Balind S, Radenović L, Prolić Z, Janać B. Age-Dependent Effects of ELF-MF on Oxidative Stress in the Brain of Mongolian Gerbils. Cell Biochem Biophys. 66(3):513-521, 2013. (AS, CE, OX)

The aim of study was to investigate the effects of extremely low frequency magnetic field (ELF-MF; 50 Hz; 0.1, 0.25 and 0.5 mT) on oxidative stress in the brain of 3- (adult) and 10-month-old (middle-aged) gerbils. Nitric oxide (NO) level, superoxide (O(2) (-)) production, superoxide dismutase (SOD) activity, and index of lipid peroxidation (ILP) were measured in the forebrain

cortex, striatum, hippocampus, and cerebellum immediately and 3 days after cessation of 7-day exposure. In all gerbils, ELF-MF significantly increased oxidative stress in all tested brain regions. This effect was correlated with the value of magnetic induction and was higher in middle-aged gerbils. Three days after cessation of exposure, the values of examined parameters were closer to control levels. In adult gerbils, the effect of ELF-MF of 0.1 mT on NO level, O(2) (-) production and SOD activity was almost fully disappeared, and ILP was at the control level regardless of the value of magnetic induction. In middle-aged gerbils, the effect of ELF-MF was still present but to a lesser degree than those observed immediately after cessation of exposure. These findings pointed out the ability of ELF-MF to induce age- and magnetic induction-dependent modification of oxidative stress in the brain.

(E) Seong Y, Moon J, Kim J. Egr1 mediated the neuronal differentiation induced by extremely low-frequency electromagnetic fields. Life Sci. 102(1):16-27, 2014. (CS, CE, MC, ND)

AIM: There is a specific frequency of extremely low-frequency electromagnetic field (ELF-EMF) that promotes neuronal differentiation. Although several mechanisms are known to regulate ELF-EMF-induced neuronal differentiation, a key factor that mediates neurogenic potentials by the ELF-EMF is largely unknown. Also, the potential use of ELF-EMF exposure in cell transplantation assays is yet to be determined, including their possible use in ELF-EMF based therapy of neurological diseases. The aim of this study is to understand the underlying mechanisms that mediate ELF-EMF-induced neuronal differentiation and also to harness these mechanisms for cell transplantation assays. MAIN METHOD: Human bone marrow-mesenchymal stem cells (hBM-MSCs) were exposed to ELF-EMF (50 Hz frequency, 1mT intensity) for 8 days. The hBM-MSC derived neurons were then analyzed by general molecular biology techniques including immunofluorescence and quantitative RT-PCR. To assess changes in gene expression induced by ELF-EMF exposure, we analyzed the transcriptome of neuronal cells after an 8-day ELF-EMF exposure (50 Hz, 1 mT) and compared the transcriptional profiles to control cells. KEY FINDING: We found that early growth response protein 1 (Egr1) is one of the key transcription factors in ELF-EMF-induced neuronal differentiation. In addition, we show that transplantations of ELF-EMF-induced neurons significantly alleviate symptoms in mouse models of neurodegenerative disease. SIGNIFICANCE: These findings indicate that a specific transcriptional factor, Egr1, mediates ELF-EMF-induced neuronal differentiations, and demonstrate the promise of ELF-EMF based cell replacement therapies for neurodegenerative diseases.

(NE) Sert C, Başak N, Koruk İ. Electric and magnetic field pollution in near substations and investigation of anxiety and depressive effects on adult individuals living in this area. Electromagn Biol Med 43:145-155, 2024. (HU, CE, BE)

Exposure to electromagnetic fields causes a variety of health problems in living systems. We investigated EMF pollution in Şanlıurfa city center and also investigated anxiety-depression symptoms in individuals (18-40 years old) exposed to this pollution. For this purpose, electric field and magnetic field measurements were taken at Electricity Distribution Center and 44 substations (for each transformer), at 0 points, 1 meter away, 2 meters away and the house/office

closest to the transformer. The experimental group was individuals living in electricity distribution center residences and individuals living near transformers (n = 55). The control group was selected from individuals who lived outside the city center of Şanlıurfa, did not have transformers or high transmission lines near their homes, and did not have any chronic diseases that could cause stress (n = 50). Anxiety and depression symptoms of the groups were measured using the Beck Anxiety Inventory Scale (BAI) and Beck Depression Inventory Scale (BDI). The relationship between EMF pollution and anxiety-depression was evaluated statistically. Maximum MF and EF values were recorded as 0.22 mT and 65.9 kV/m, respectively. All measured MF values were below standards, but EF values were above standards at some points. In conclusion, there is no statistically convincing evidence of a relationship between EMF exposure and anxiety-depression ($p > 0.05$). This result shows that there may be more meaningful results in places with higher EMF levels. We interpreted the fact that exposure to electromagnetic fields does not cause anxiety and depression in individuals, as the measured values are below the limit values.

(E) Shabani Z, Nejad DM, Ghadiri T, Karimipour M. Evaluation of the neuroprotective effects of Vitamin E on the rat substantia nigra neural cells exposed to electromagnetic field: An ultrastructural study. Electromagn Biol Med40(3):428-437, 2021. (AS, CE, MC, CC, OX, MA, ND, IX)

Electromagnetic fields (EMFs) could induce oxidative stress (OS) in human tissues. Lipid peroxidation (LPO) is the main hallmark of OS that harms neural cell components, primarily lipids in the myelin sheaths and membranes. Vitamin E is a lipophilic antioxidant that protects cells from OS-related damages and inhibits the LPO process. In this study, male rats were assigned into three groups of Control, EMF, and EMF+ Vitamin E. The EMF producer equipment produced an alternate current of 50 Hz, 3 Mili Tesla (mT). At the end of the experiment, half of the substantia nigra in every sample was used for measurement of the malondialdehyde (MDA) level as the end-product of the LPO and activity of superoxide dismutase (SOD) enzyme. The next half of the tissue was prepared for transmission electron microscopy (TEM). In the EMF group, MDA level was enhanced and SOD value decreased significantly compared to the control group, but Vitamin E could restore these changes. In rats undergone EMF, heterochromatic nucleus and destruction in some portions of the nuclear membrane were detected. The segmental separation or destruction of myelin sheath lamellae was observed in nerve fibers. In treated animals, the nucleus was round, less heterochromatic, with a regular membrane. Separation of myelin sheath lamellae in some nerve fibers was slighter than the radiation group. Considering the results, EMF exposure induces LPO and triggers ultrastructural changes in the cell membranes, nucleus, and myelin sheath of substantia nigra cells, but Vitamin E consumption weakens these neuropathological alterations.

(E) Shafiei SA, Firoozabadi SM, Rasoulzadeh Tabatabaie K, Ghabaee M. Study of the frequency parameters of EEG influenced by zone-dependent local ELF-MF exposure on the human head. Electromagn Biol Med. 31(2):112-12, 2012. (HU, AE, EE)

It has been reported that human subjects exposed to electromagnetic fields exhibit changes in human EEG signals at the frequency of stimulation. The aim of the present study was to expose different parts of the brain to extremely low-frequency magnetic fields locally and investigate

EEG power spectrum alters at the frequency of stimulation. EEG relative power spectrum were evaluated at 3, 5, 10, 17, and 45 Hz frequencies at T4, T3, F3, Cz, and F4 points, respectively, when these points were exposed to magnetic fields with similar frequencies and 100 µT intensity. The paired t-test results showed that power value of EEG did not alter significantly at the frequency of stimulation (P<0.05). Further, significant changes in different EEG bands caused by locally exposing to ELF-MF in different points of brain were observed. The changes in the EEG bands were not limited necessarily to the exposure point.

(E) Shafiei SA, Firoozabadi SM, Tabatabaie KR, Ghabaee M. Investigation of EEG changes during exposure to extremely low-frequency magnetic field to conduct brain signals. Neurol Sci. 35(11):1715-1721, 2014. (HU, AE, EE)

There are evidences that confirm the effect of magnetic fields (MFs) on brain signals and some psychological disorders such as headache, migraine and depression. The aim of the present study was to investigate changes in EEG power spectrum due to localized exposure in different parts of the brain by extremely low-frequency magnetic fields (ELF-MFs) to extract some protocols for treatment of some psychological disorders. In addition, regular effects were investigated by increasing intensity of ELF-MF. Therefore, EEG relative power spectrum was evaluated at T4, T3, F3, F4, and Cz points, when all the points were exposed to MFs with 45, 17, 10, 5, and 3 Hz frequencies, separately. Intensity of MF was 0, 100, 240, or 360 µT in four sessions. Significant changes were observed in different EEG bands caused by locally exposing to ELF-MF in different points of brain (P < 0.05). Some exposure to MFs decreased alpha band of frontal and central areas in closed-eyes state. Based on the findings in this study, some protocols can be designed using a combination of various MFs exposures to conduct the brain signals that is necessary to evaluate clinically.

(E) Shahbazi-Gahrouei D, Shiri L, Alaei H, Naghdi N.The effect of continuous ELF-MFs on the level of 5-HIAA in the raphe nucleus of the rat. J Radiat Res. 57:127-132, 2016. (AS, CE, CC, MA)

The aim of this study was to investigate the effect of continuous extremely low frequency magnetic fields (ELF-MFs) with a frequency of 10 Hz and an intensity of 690-720 µT on the level of 5-hydroxyindolacetic acid (5-HIAA) in adult male Wistar rats. A total of 24 adult Wistar male rats were used, and after exposure with an ELF-MF for 15 successive days, all rats in each test were anesthetized with chloral hydrate. Then, they were placed in a stereotaxic frame for surgery and a microdialysis process. Dialysate samples were analyzed to measure the amount of 5-HIAA by high performance liquid chromatography (HPLC) using electrochemical detection. Results showed that ELF-MF exposure for 15 days, 1 h daily, was not effective in altering the level of 5-HIAA. However, ELF-MF exposure for 15 days, 3 h daily, decreased the level of the 5-HIAA in the raphe nucleus. It can be concluded that ELF-MFs affect the serotonergic system and may be used to treat nervous system diseases. This study is an initial step towards helping cure depression using ELF-MFs.

(E) Shen JF, Chao YL, Du L. Effects of static magnetic fields on the voltage-gated potassium channel currents in trigeminal root ganglion neurons. Neurosci Lett. 415(2):164-168, 2007. (CS, AE, CC, FC)

To evaluated the effects of moderate-intensity static magnetic fields (SMF) on two types of voltage-gated potassium channel (VGPC) currents: I(K,A) and I(K,V), whole-cell patch-clamp experiments were conducted on acute dissociated rat trigeminal root ganglion (TRG) neurons. The results demonstrated that 125 mT SMF could influence the inactivation kinetics of these two VGPC currents by altering the inactivation rate and velocity. No significant change was observed in the activation properties. These findings supported the hypothesis that biological membrane would be deformed in moderate-intensity SMF and the physiological characteristics of ion channels on the membrane would be influenced. The mechanism underlying the different effects of SMF on the I(K,A) and I(K,V) inactivation was also discussed.

(E) Shepherd S, Hollands G, Godley VC, Sharkh SM, Jackson CW, Newland PL. Increased aggression and reduced aversive learning in honey bees exposed to extremely low frequency electromagnetic fields. PLoS One. 14(10):e0223614, 2019. (AS, BE)

Honey bees, Apis mellifera, are a globally significant pollinator species and are currently in decline, with losses attributed to an array of interacting environmental stressors. Extremely low frequency electromagnetic fields (ELF EMFs) are a lesser-known abiotic environmental factor that are emitted from a variety of anthropogenic sources, including power lines, and have recently been shown to have a significant impact on the cognitive abilities and behaviour of honey bees. Here we have investigated the effects of field-realistic levels of ELF EMFs on aversive learning and aggression levels, which are critical factors for bees to maintain colony strength. Bees were exposed for 17 h to 100 μT or 1000 μT ELF EMFs, or a sham control. A sting extension response (SER) assay was conducted to determine the effects of ELF EMFs on aversive learning, while an intruder assay was conducted to determine the effects of ELF EMFs on aggression levels. Exposure to both 100 μT and 1000 μT ELF EMF reduced aversive learning performance by over 20%. Exposure to 100 μT ELF EMFs also increased aggression scores by 60%, in response to intruder bees from foreign hives. These results indicate that short-term exposure to ELF EMFs, at levels that could be encountered in bee hives placed under power lines, reduced aversive learning and increased aggression levels. These behavioural changes could have wider ecological implications in terms of the ability of bees to interact with, and respond appropriately to, threats and negative environmental stimuli.

Shibata T, Hattori N, Nishijo H, Kuroda S, Takakusaki K. The origins of light-independent magnetoreception in humans. Front Hum Neurosci 18:1482872, 2024. (Review)

The Earth's abundance of iron has played a crucial role in both generating its geomagnetic field and contributing to the development of early life. In ancient oceans, iron ions, particularly around deep-sea hydrothermal vents, might have catalyzed the formation of macromolecules, leading to the emergence of life and the Last Universal Common Ancestor. Iron continued to influence catalysis, metabolism, and molecular evolution, resulting in the creation of magnetosome gene clusters in magnetotactic bacteria, which enabled these unicellular organisms to detect geomagnetic field. Although humans lack a clearly identified organ for geomagnetic

sensing, many life forms have adapted to geomagnetic field-even in deep-sea environments-through mechanisms beyond the conventional five senses. Research indicates that zebrafish hindbrains are sensitive to magnetic fields, the semicircular canals of pigeons respond to weak potential changes through electromagnetic induction, and human brainwaves respond to magnetic fields in darkness. This suggests that the trigeminal brainstem nucleus and vestibular nuclei, which integrate multimodal magnetic information, might play a role in geomagnetic processing. From iron-based metabolic systems to magnetic sensing in neurons, the evolution of life reflects ongoing adaptation to geomagnetic field. However, since magnetite-activated, torque-based ion channels within cell membranes have not yet been identified, specialized sensory structures like the semicircular canals might still be necessary for detecting geomagnetic orientation. This mini-review explores the evolution of life from Earth's formation to light-independent human magnetoreception, examining both the magnetite hypothesis and the electromagnetic induction hypothesis as potential mechanisms for human geomagnetic detection.

(E) Shin EJ, Jeong JH, Kim HJ, Jang CG, Yamada K, Nabeshima T, Kim HC. Exposure to extremely low frequency magnetic fields enhances locomotor activity via activation of dopamine D1-like receptors in mice. J Pharmacol Sci. 105(4):367-371, 2007. (AS, AE, CE, BE, CC)

We demonstrated that exposure to extremely low frequency magnetic fields (ELF-MF) enhanced dopamine levels in the rat striatum. To extend our understanding, we examined the role of dopaminergic receptors in ELF-MF-induced behavioral changes. Exposure to ELF-MF (2.4 mT, 1 h/day, for one or seven days) enhanced locomotor activity in a time-dependent manner. This hyperlocomotor activity paralleled an increase in c-Fos-like immunoreactivity (c-Fos-IR). Pretreatment with SCH23390, a dopaminergic D(1)-like receptor antagonist, but not with sulpiride, a dopaminergic D(2)-like receptor antagonist, inhibited ELF-MF-induced increased locomotor activity and c-Fos-IR. Thus, our results suggest that ELF-MF-induced behavioral responses are, at least in part, mediated by activation of dopamine D(1)-like receptors.

(E) Shin EJ, Nguyen XK, Nguyen TT, Pham DT, Kim HC. Exposure to extremely low frequency magnetic fields induces fos-related antigen-immunoreactivity via activation of dopaminergic D1 receptor. Exp Neurobiol. 20(3):130-6, 2011. (CE, BE, CC)

We previously demonstrated that repeated exposure to extremely low frequency magnetic fields (ELF-MF) increases locomotor activity via stimulation of dopaminergic D1 receptor (J. Pharmacol. Sci., 2007;105:367-371). Since it has been demonstrated that activator protein-1 (AP-1) transcription factors, especially 35-kDa fos-related antigen (FRA), play a key role in the neuronal and behavioral adaptation in response to various stimuli, we examined whether repeated ELF-MF exposure induces FRA-immunoreactivity (FRA-IR) in the striatum and nucleus accumbens (striatal complex) of the mice. Repeated exposure to ELF-MF (0.3 or 2.4 mT, 1 h/day, for consecutive fourteen days) significantly induced hyperlocomotor activity and FRA-IR in the striatal complex in a field intensity-dependent manner. ELF-MF-induced FRA-IR lasted for at least 1 year, while locomotor activity returned near control level 3 months after the final exposure to ELF-MF. Pretreatment with SCH23390, a dopaminergic D1 receptor antagonist, but not with sulpiride, a dopaminergic D2 receptor antagonist, significantly attenuated

hyperlocomotor activity and FRA-IR induced by ELF-MF. Our results suggest that repeated exposure to ELF-MF leads to prolonged locomotor stimulation and long-term expression of FRA in the striatal complex of the mice via stimulation of dopaminergic D1 receptor.

(E) Shuo T, Yumeng Y, Leilei Y, Yanhui H, Chao Y, Hua Y, X, Zhaoqian J, Cuicui H, Hongyan Z, Yang L. Static magnetic field induces abnormality of glucose metabolism in rats' brain and results in anxiety-like behavior. J Chem Neuroanat. 113:101923, 2021. (AS, CE, CC, BE)

In this study, fifty-four male Wistar rats were randomly divided into four groups according to the static magnetic field (SMF) intensity, namely, control, low-intensity, moderate-intensity, and high-intensity groups. The rats' whole body was exposed to a superconducting magnet exposure source. The exposure SMF intensity for the low-intensity, moderate-intensity, and high-intensity groups was 50 m T, 100 m T, and 200 m T, respectively, and the exposure time was 1 h/day for consecutive 15 days. After different exposure times, glucose metabolism in rats' brain was evaluated by micro-positron emission tomography (micro-PET), and the expression of hexokinase 1(HK1) and 6-phosphate fructokinase-1(PFK1) was detected by western blot. The exploration and locomotion abilities of the rats were evaluated by conducting open field test (OFT). Furthermore, pathological changes of rats' brain were observed under a microscope by using hematoxylin-eosin staining. PET results showed that moderate-intensity SMFs could cause fluctuant changes in glucose metabolism in rats' brain and the abnormalities were SMF intensity dependent. The expression of the two rate-limiting enzymes HK1 and PFK1 in glucose metabolism in brain significantly decreased after SMF exposure. The OFT showed that the total distance, surrounding distance, activity time, and climbing and standing times significantly decreased after SMF exposure. The main pathological changes in the brain were pyknosis, edema of neurons, and slight widening of the perivascular space, which occurred after 15 times of exposure. This study indicated that SMF exposure could lead to abnormal glucose metabolism in the brain and might result in anxiety-like behaviors.

(E) Sieroń A, Brus R, Szkilnik R, Plech A, Kubański N, Cieślar G. Influence of alternating low frequency magnetic fields on reactivity of central dopamine receptors in neonatal 6-hydroxydopamine treated rats. Bioelectromagnetics. 22(7):479-486, 2001. (AS, CE, FC)

The aim of this study was to evaluate the influence of extremely low frequency magnetic field (ELF MF) on the reactivity of the central dopamine D(1) receptor in rats with dopamine neurons chemically damaged by 6-hydroxydopamine (6-OHDA), an animal model of human's Parkinson's disease. The experiment was carried out on male Wistar rats. On day 3 of postnatal life, a lasting and selective chemical damage of the central dopamine system was induced in the rats by infusion of 6-OHDA HBr (133.4 microg intracerebroventricular, base form) given bilaterally into lateral ventricles of the brain. Control animals received similar treatments injecting only vehicle. At 2 months of age, both 6-OHDA treated and control rats were randomly divided into two groups. Rats from the first group were exposed to 10 Hz sinusoidal, 1.8-3.8 mT magnetic field one hour daily for 14 days. Rats of the second group were sham exposed, with the applicator solenoid turned off. On the day after the final exposure the evaluations were made of

the rat's spontaneous irritability, oral activity, and catalepsy. The MF exposed rat with chemically induced dopamine neurons damage exhibited a reduction of irritability and oral activity when stimulated with SKF 38393 (the agonist of central dopamine D(1) receptor) and some increase of catalepsy after administration of SCH 23390(the antagonist of central dopamine D(1) receptor). These results indicate that ELF MF reduce the reactivity of central dopamine D(1) receptors in rats.

(E) Sissons SM, Dotta BT. Brain structure alterations following neonatal exposure to low-frequency electromagnetic fields: A histological analysis. Int J Dev Neurosci 2024 Jul 5. doi: 10.1002/jdn.10361. Online ahead of print. (AS, CE, MC, DE, IX)

Nitric oxide (NO) and electromagnetic fields (EMF) have been extensively studied for their roles in neurobiology, particularly in regulating cerebral functions and synaptic plasticity. This study investigates the impact of EMFs on NO modulation and its subsequent effects on neurodevelopment, building upon prior research examining EMF exposure's consequences on Wistar albino rats. Rats were exposed perinatally to either tap water, 1 g/L of L-arginine (LA) or 0.5 g/L of N-methylarginine (NMA). Half of the rats in each group were also exposed to a 7-Hz square-wave EMF at three separate intensities (5, 50 and 500 nT) for 2-14 days following birth. Animals were allowed to develop, and their brains were harvested later in adulthood (mean age = 568.17 days, SD = 162.73). Histological analyses were used to elucidate structural changes in key brain regions. All brains were stained with Toluidine Blue O (TBO), enabling the visualization of neurons. Neuronal counts were then conducted in specific regions of interest (e.g. hippocampus, cortices, amygdala and hypothalamus). Histological analyses revealed significant alterations in neuronal density in specific brain regions, particularly in response to EMF exposure and pharmacological interventions. Notable findings include a main EMF exposure effect where increased neuronal counts were observed in the secondary somatosensory cortex under low EMF intensities ($p < 0.001$) and sex-specific responses in the hippocampus, where a significant increase in neuronal counts was observed in the left CA3 region in female rats exposed to EMF compared to unexposed females ($t(18) = 2.371$, $p = 0.029$). Additionally, a significant increase in neuronal counts in the right entorhinal cortex was seen in male rats exposed to EMF compared to unexposed males ($t(18) = 2.216$, $p = 0.040$). These findings emphasize the complex interaction among sex, EMF exposure and pharmacological agents on neuronal dynamics across brain regions, highlighting the need for further research to identify underlying mechanisms and potential implications for cognitive function and neurological health in clinical and environmental contexts.

(NE) Sorahan T, Mohammed N. Neurodegenerative disease and magnetic field exposure in UK electricity supply workers. Occup Med (Lond). 64(6):454-460, 2014. (CE, HU, ND)

BACKGROUND: Previous research has suggested a possible link between neurodegenerative disease and exposure to extremely low-frequency electric and magnetic fields. AIMS: To investigate whether risks of Alzheimer's, motor neurone or Parkinson's disease are related to occupational exposure to magnetic fields. METHODS: The mortality experienced by a cohort of

73051 employees of the former Central Electricity Generating Board of England and Wales was investigated for the period 1973-2010. All employees were hired in the period 1952-82, were employed for at least 6 months and had some employment after 1 January 1973. Detailed calculations had been performed by others to enable an assessment to be made of exposures to magnetic fields. Poisson regression was used to calculate relative risks (rate ratios) of developing any of the three diseases under investigation for categories of lifetime, distant (lagged) and recent (lugged) exposure. RESULTS: No statistically significant trends were shown for risks of any of these diseases to increase with estimates of lifetime, recent or distant exposure to magnetic fields. CONCLUSIONS: There is no convincing evidence that UK electricity generation and transmission workers have suffered elevated risks from neurodegenerative diseases as a consequence of exposure to magnetic fields.

(NE) Sorahan T, Nichols L Motor neuron disease risk and magnetic field exposures. Occup Med (Lond) 72(3):184-190, 2022. (HU, CE, ND)

Background: Many studies have investigated magnetic field exposure and the risks of motor neuron disease (MND). Meta-analyses have found positive associations but a causal relationship has not been established. **Aims:** To investigate the risks of MND and occupational exposure to magnetic fields in a large UK cohort. **Methods:** Mortality of 37 986 employees of the former Central Electricity Generating Board of England and Wales was investigated for the period 1987-2018. Employees were first employed in the period 1942-82 and were still in employment on the 1 November, 1987. Detailed calculations enabled estimates to be made of magnetic field exposures. Observed deaths were compared with expected numbers based on mortality rates for the general population of England and Wales and Poisson regression was used to calculate rate ratios (relative risks) for categories of lifetime, lagged (distant) and lugged (recent) magnetic field exposure. **Results:** Mortality from MND in the total cohort was similar to national rates (observed 69, expected 71.3, SMR 97, 95% CI 76-122). There were no statistically significant trends of risks increasing with lifetime, recent or distant magnetic field exposure, although positive associations were observed for some categories of recent exposure. **Conclusions:** The study did not find that the cohort had elevated risks of MND as a consequence of occupational lifetime exposure to magnetic fields, although a possible role for recent exposures could usefully be investigated in other datasets.

(E) Spasić S, Kesić S, Stojadinović G, Petković B, Todorović D. Effects of the static and ELF magnetic fields on the neuronal population activity in Morimus funereus (Coleoptera, Cerambycidae) antennal lobe revealed by wavelet analysis. Comp Biochem Physiol A Mol Integr Physiol. 181-27-35, 2015. (AS, AE, EE)

To study the influence of a static magnetic field (SMF, 2mT) and extremely low frequency magnetic field (ELF MF, 50Hz, 2mT) on the neuronal population activity, the experiments were performed on adult longhorn beetles Morimus funereus (Coleoptera, Cerambycidae). Based on a wavelet analysis of the local field potentials (LFPs), our study showed for the first time that the effects of prolonged and repeated exposure to the ELF MF on the LFPs were irreversible within investigated time frame. The relative wavelet energy (RWE) of 4-8Hz frequency band was

significantly increased after sine ELF MF (SnMF)/square ELF MF (SqMF) in comparison to the control value. The RWE of slower oscillations (1-2Hz) was significantly decreased after the repeated exposures to either SnMF or SqMF. The SqMF induced decreasing of the faster waves in the range of 64-128Hz. However, we did not prove with presented methods that exposure to the SMF for 5min produces any effects on the neuronal population activity. This study has proved the wavelet transform as a valuable tool for measuring the effects of SMF and ELF MF on the neuronal population activity in M. funereus antennal lobe.

Stam R. Low frequency magnetic field exposure and neurodegenerative disease: systematic review of animal studies. Electromagn Biol Med. 2025 Aug 3:1-15. doi: 10.1080/15368378.2025.2540435. Epub ahead of print. (Review)

Epidemiological studies have found an association between occupational exposure to low frequency magnetic fields and the occurrence of motor neuron disease and Alzheimer's disease. No association has been found for Parkinson's disease and the evidence for multiple sclerosis is insufficient. Animal models studying the effects of low frequency magnetic fields on neurodegenerative disease induction or progression could provide more evidence on causation and the underlying mechanisms. A systematic search and review was conducted of peer-reviewed research articles involving animal experiments on the effects of low frequency magnetic field exposure on behavioural and neuroanatomical outcomes relevant for neurodegenerative diseases in humans. Firstly, experimental studies in *naive animals* do not support a causal relationship between exposure to low frequency magnetic fields and the induction of neuropathology relevant for Alzheimer's disease, but the number of studies relevant for motor neuron disease, multiple sclerosis and Parkinson's disease is too limited to draw conclusions. Secondly, experimental studies in *existing animal models for neurodegenerative disease* support a therapeutic (beneficial) effect of low frequency magnetic field treatment on behavioural and neuroanatomical abnormalities relevant for dementia (including Alzheimer's disease), multiple sclerosis and Parkinson's disease and no effect on disease progression in models relevant for motor neuron disease.

(E) Stevens P. Affective response to 5 microT ELF magnetic field-induced physiological changes. Bioelectromagnetics. 28(2):109-114, 2007. (HU, AE, BE)

Research into effects of weak magnetic fields (MFs) at biologically relevant frequencies has produced ambiguous results. Although they do affect human physiology and behaviour, the direction of effects is inconsistent, with a range of complex and unrelated behaviours being susceptible. A possible explanation is that these effects, rather than being directly caused, are instead related to changes in affective state. A previous study showed that MFs altered the affective content of concurrent perceptions, but it was unclear whether the emotional response was direct or indirect. Here it is shown that exposure to a 0-5 microT MF (DC-offset sinudsoidal wave form) within EEG alpha-band frequencies (8-12 Hz), results in a reported change in emotional state. This relates to a decrease global field power but lacks the frontal alpha-asymmetry that would physiologically indicate a directly induced emotional state, suggesting that participant experiences are due to an interpretation of the effects of MF exposure.

(E) Strasák L, Bártová E, Krejci J, Fojt L, Vetterl V. Effects of ELF-EMF on brain proteins in mice. Electromagn Biol Med. 28(1):96-104, 2009. (AS, AE, CC)

Effect of electromagnetic low frequency fields was studied on mice. We analyzed level of protein in brain of mouse. The levels of c-Jun and c-Fos in brains were measured using Western-blot techniques. Female and male laboratory mice were exposed for 4 days to magnetic field (Bm = 2 mT, f = 50 Hz). The exposure took place in cylindrical coil at laboratory temperature. After the experiment they were sacrificed and the level of protein c-Jun and c-Fos in different parts of brain were estimated. The expression of c-Fos was not affected by magnetic field on the other hand the expression of c-Jun decreased after magnetic field exposure. The results did not depend on sex of mice.

(E) Sun H, Che Y, Liu X, Zhou D, Miao Y, Ma Y. Effects of prenatal exposure to a 50-Hz magnetic field on one-trial passive avoidance learning in 1-day-old chicks. Bioelectromagnetics. 31(2):150-155, 2010. (AS, CE, BE, DE)

We investigated memory impairment in newly hatched chicks following in ovo exposure to a 50-Hz magnetic field (MF) of 2 mT (60 min/day) on embryonic days 12-18. Isolated and paired chicks were used to test the effect of stress during training, and memory retention was tested at 10, 30, and 120 min, following exposure to a bitter-tasting bead (100% methylanthranilate). Results showed that memory was intact at 10 min in both isolated and paired chicks with or without MF exposure. However, while isolated chicks had good memory retention levels at 30 and 120 min, those exposed to MF did not. The results suggest a potential disruption of memory formation following in ovo exposure to MF, with this effect only evident in the more stressed, isolated chicks.

(E) Sun ZC, Ge JL, Guo B, Guo J, Hao M, Wu YC, Lin YA, La T, Yao PT, Mei YA, Feng Y, Xue L. Extremely Low Frequency Electromagnetic Fields Facilitate Vesicle Endocytosis by Increasing Presynaptic Calcium Channel Expression at a Central Synapse. Sci Rep. 6:21774, 2016. (AS, CE, FC)

Accumulating evidence suggests significant biological effects caused by extremely low frequency electromagnetic fields (ELF-EMF). Although exo-endocytosis plays crucial physical and biological roles in neuronal communication, studies on how ELF-EMF regulates this process are scarce. By directly measuring calcium currents and membrane capacitance at a large mammalian central nervous synapse, the calyx of Held, we report for the first time that ELF-EMF critically affects synaptic transmission and plasticity. Exposure to ELF-EMF for 8 to 10 days dramatically increases the calcium influx upon stimulation and facilitates all forms of vesicle endocytosis, including slow and rapid endocytosis, endocytosis overshoot and bulk endocytosis, but does not affect the RRP size and exocytosis. Exposure to ELF-EMF also potentiates PTP, a form of short-term plasticity, increasing its peak amplitude without impacting its time course. We further investigated the underlying mechanisms and found that calcium channel expression, including the P/Q, N, and R subtypes, at the presynaptic nerve terminal was enhanced, accounting for the increased calcium influx upon stimulation. Thus, we conclude that

exposure to ELF-EMF facilitates vesicle endocytosis and synaptic plasticity in a calcium-dependent manner by increasing calcium channel expression at the nerve terminal.

(E) Szemerszky R, Zelena D, Barna I, Bárdos G. Stress-related endocrinological and psychopathological effects of short- and long-term 50Hz electromagnetic field exposure in rats. Brain Res Bull. 81(1):92-99, 2010. (AS, CE, BE, CC)

It is believed that different electromagnetic fields do have beneficial and harmful biological effects. The aim of the present work was to study the long-term consequences of 50 Hz electromagnetic field (ELF-EMF) exposure with special focus on the development of chronic stress and stress-induced psychopathology. Adult male Sprague-Dawley rats were exposed to ELF-EMF (50 Hz, 0.5 mT) for 5 days, 8h daily (short) or for 4-6 weeks, 24h daily (long). Anxiety was studied in elevated plus maze test, whereas depression-like behavior of the long-treated group was examined in the forced swim test. Some days after behavioral examination, the animals were decapitated among resting conditions and organ weights, blood hormone levels as well as proopiomelanocortin mRNA level from the anterior lobe of the pituitary gland were measured. Both treatments were ineffective on somatic parameters, namely none of the changes characteristic to chronic stress (body weight reduction, thymus involution and adrenal gland hypertrophy) were present. An enhanced blood glucose level was found after prolonged ELF-EMF exposure ($p=0.013$). The hormonal stress reaction was similar in control and short-term exposed rats, but significant proopiomelanocortin elevation ($p<0.000$) and depressive-like behavior (enhanced floating time; $p=0.006$) were found following long-term ELF-EMF exposure. Taken together, long and continuous exposure to relatively high intensity electromagnetic field may count as a mild stress situation and could be a factor in the development of depressive state or metabolic disturbances. Although we should stress that the average intensity of the human exposure is normally much smaller than in the present experiment.

(E)
Tachibana M, Inada T, Kimura H, Ito M, Kuwatsuka Y, Kinoshita F, Mori D, Ohno K. Extremely Low Frequency, Extremely Low Magnetic Environment for depression: An open-label trial. Asian J Psychiatr 96:104036, 2024. (CE, HU, BE, MA)

Mitochondrial dysfunction has been suggested to play a role in depression pathogenesis. This clinical trial (jRCTs042220011) was conducted to evaluate whether depression symptoms could be alleviated by an Extremely Low Frequency, Extremely Low Magnetic Environment (ELF-ELME), which has been found in basic research studies to enhance mitochondrial membrane potential. Participants were exposed to the ELF-ELME via a head-mounted magnetic field device (10 µTesla, 4 ms, 1-8 Hz/8 s) worn for 2 h per day for 8 consecutive weeks. Four male patients with treatment-resistant depression were enrolled. Significant reductions from baseline in the average total Montgomery-Åsberg Depression Rating Scale (MADRS) score were observed at 4, 6, and 8 weeks. ELF-ELME appears to ameliorate depressive symptoms in patients with major depressive disorder safely and effectively, suggesting that it could be used as an alternative treatment for depressive patients who do not prefer to take antidepressants and in combination with antidepressant therapy for patients who only partially respond to pharmacotherapy.

(E) Tadres D, Riedl J, Eden A, Bontempo AE, Lin J, Reid SF, Roehrich B, Williams K, Sepunaru L, Louis M. Sensation of electric fields in the Drosophila melanogaster larva. Curr Biol. 28:S0960-9822(25)00299-4, 2025. (AS, AE, BE, EF)

Electrosensation has emerged as a crucial sensory modality for social communication, foraging, and predation across the animal kingdom. However, its presence and functional role as well as the neural basis of electric field perception in Drosophila and other invertebrates remain unclear. In environments with controlled electric fields, we identified electrosensation as a new sense in the Drosophila melanogaster larva. We found that the Drosophila larva performs robust electrotaxis: when exposed to a uniform electric field, larvae migrate toward the cathode (negatively charged elecrode) and quickly respond to changes in the orientation of the field to maintain cathodal movement. Through a behavioral screen, we identified a subset of sensory neurons located at the tip of the larval head that are necessary for electrotaxis. Calcium imaging revealed that a pair of Gr66a-positive sensory neurons (one on each side of the head) encodes the strength and orientation of the electric field. Our results indicate that electric fields elicit robust behavioral and neural responses in the Drosophila larva, providing new evidence for the significance of electrosensation in invertebrates.

(NE) Taormina B, Di Poi C, Agnalt A-L, Carlier A, Desroy N, Escobar-Lux RH, Jean-François D'eu J-F, Freyte F, Durif CMF. Impact of magnetic fields generated by AC/DC submarine power cables on the behavior of juvenile European lobster (Homarus gammarus). Aquat Toxicol 220:105401, 2020. (VO, CE, BE)

The number of submarine power cables using either direct or alternating current is expected to increase drastically in coming decades. Data concerning the impact of magnetic fields generated by these cables on marine invertebrates are scarce. In this context, the aim of this study was to explore the potential impact of anthropogenic static and time-varying magnetic fields on the behavior of recently settled juvenile European lobsters (Homarus gammarus) using two different behavioral assays. Day-light conditions were used to stimulate the sheltering behavior and facilitate the video tracking. We showed that juvenile lobsters did not exhibit any change of behavior when submitted to an artificial magnetic field gradient (maximum intensity of 200 μT) compared to non-exposed lobsters in the ambient magnetic field. Additionally, no influence was noted on either the lobsters' ability to find shelter or modified their exploratory behavior after one week of exposure to anthropogenic magnetic fields (225 ± 5 μT) which remained similar to those observed in control individuals. It appears that static and time-varying anthropogenic magnetic fields, at these intensities, do not significantly impact the behavior of juvenile European lobsters in daylight conditions. Nevertheless, to form a complete picture for this biological model, further studies are needed on the other life stages as they may respond differently.

(NE) Tasić T, Lozić M, Glumac S, Stanković M, Milovanovich I, M Djordjevich M, Trbovich AM, Japundžić-Žigon N, De Luka SR. Static magnetic field on behavior, hematological parameters and organ damage in spontaneously hypertensive rats. Ecotoxicol Environ Saf. 207:111085, 2020. (AS, CE, BE)

Previous studies showed contradictory results of static magnetic field (SMF) influence on behavior, hematological parameters and organ damage. The aim of this study was to investigate influence of subchronic continuous exposure to upward and downward oriented SMF of moderate intensity on behavior, hematological characteristics, heart and kidney tissue of spontaneously hypertensive rats. SH rats exposed to downward oriented SMF demonstrated lack of anxious-like behavior. SMF of either orientation caused decrease in the number of platelets in peripheral blood, granulocytes in the spleen and bone marrow and increase in the number of erythrocytes in the spleen, in both exposed groups. We also demonstrated that spontaneously hypertensive rats exposed to upward oriented SMF exhibited decreased lymphocytes count in blood, decreased bone marrow erythrocytes count and rats exposed to downward oriented SMF had increased lymphocytes count in bone marrow. The results showed adverse effect of differently oriented SMF on hematological parameters of spontaneously hypertensive rats. Also, exposure to different oriented SMF didn't affect their heart and kidney morphological characteristics.

(E) Tasset I, Medina FJ, Jimena I, Agüera E, Gascón F, Feijóo M, Sánchez-López F, Luque E, Peña J, Drucker-Colín R, Túnez I. Neuroprotective effects of extremely low-frequency electromagnetic fields on a Huntington's disease rat model: effects on neurotrophic factors and neuronal density. Neuroscience. 209:54-63, 2012. (AS, CE, MC, CC, BE, OX, MA, ND)

There is evidence to suggest that the neuroprotective effect of exposure of extremely low-frequency electromagnetic fields (ELF-EMF) may be due, at least in part, to the effect of these fields on neurotrophic factors levels and cell survival, leading to an improvement in behavior. This study was undertaken to investigate the neuroprotective effects of ELFEF in a rat model of 3-nitropropionic acid (3NP)-induced Huntington's disease. Behavior patterns were evaluated, and changes in neurotrophic factor, cell damage, and oxidative stress biomarker levels were monitored in Wistar rats. Rats were given 3NP over four consecutive days (20 mg/kg body weight), whereas ELFEF (60 Hz and 0.7 mT) was applied over 21 days, starting after the last injection of 3NP. Rats treated with 3NP exhibited significantly different behavior in the open field test (OFT) and the forced swim test (FST), and displayed significant differences in neurotrophic factor levels and oxidative stress biomarkers levels, together with a neuronal damage and diminished neuronal density, with respect neuronal controls. ELFEF improved neurological scores, enhanced neurotrophic factor levels, and reduced both oxidative damage and neuronal loss in 3NP-treated rats. ELFEF alleviates 3NP-induced brain injury and prevents loss of neurons in rat striatum, thus showing considerable potential as a therapeutic tool.

(E) Tasset I, Pérez-Herrera A, Medina FJ, Arias-Carrión O, Drucker-Colín R, Túnez I. Extremely low-frequency electromagnetic fields activate the antioxidant pathway Nrf2 in a Huntington's disease-like rat model. Brain Stimul. 6:84-86, 2013.

Transcranial magnetic stimulation (TMS) is a non-invasive technique used recently to treat different neuropsychiatric and neurodegenerative disorders. Despite its proven value, the mechanisms through which TMS exerts its beneficial action on neuronal function remain

unclear. Recent studies have shown that its beneficial effects may be at least partly due to a neuroprotective effect on oxidative and cell damage. This study shows that TMS can modulate the Nrf2 transcriptor factor in a Huntington's disease-like rat model induced by 3-nitropropionic acid (3-NP). Western blot analysis demonstrated that 3-NP caused a reduction in Nrf2 in both cytoplasm and nucleus, while TMS applied to 3-NP-treated rats triggered an increase in cytoplasm and nucleus Nrf2 levels. It was therefore concluded that TMS modulates Nrf2 expression and translocation and that these mechanisms may partly explain the neuroprotective effect of TMS, as well as its antioxidant and cell protection capacity.

(E) Téglás T, Dörnyei G, Bretz K, Nyakas C. Whole-body pulsed EMF stimulation improves cognitive and psychomotor activity in senescent rats. Behav Brain Res 349:163-168, 2018. (AS, CE. BE, MA)

During advanced aging passive exercise (PE) is becoming a valuable therapeutic intervention to improve physical and mental performances. In the present study chronic low frequency pulsed electromagnetic field (EMF) exposure was presented to senescent rats in order to clarify the behavioural effects related to cognitive and motility functions. Male Wistar rats of 30-32 months old were treated with EMF for six weeks, 3 times per week, 24 min per sessions prior to the age of 32 months. Stimulation intensities varied from 45 to 1250 µT. Psychomotility was estimated in an open field (OF), attention ability in novel object recognition (NOR), and spatial learning in the Morris water maze (MWM) tests. The results showed that EMF stimulation enhanced novelty-induced motility of vertical type, i.e. frequency of rearing activity was increased. In the cognitive tests EMF exposure increased attention-based discrimination in NOR and facilitated working memory type of spatial learning in the MWM tests. No undesirable type of side effects could be obtained even after the highest dose used. It is concluded that EMF stimulation in senescent age supports cognitive and psychomotor function in rats. The notion that PE may have complementary beneficial action on brain and motor functions in senescent age is strengthened by the present experimental results.

(NE) Tekam CKS, Shreyasi Majumdar, Pooja Kumari, Santosh Kumar Prajapati, Ajay Kumar Sahi, Saksha Shinde, Richa Singh, Puneet Kumar Samaiya, Ranjana Patnaik, Sairam Krishnamurthy, Sanjeev Kumar Mahto. Effects of ELF-PEMF Exposure on Spontaneous Alternation, Anxiety, Motor Co-ordination and Locomotor Activity of Adult Wistar Rats and Viability of C6 (Glial) Cells in Culture. Toxicology 485:153409, 2023. (AS, CE, BE)

The effects of ELF-PEMF exposure on spontaneous alternation, anxiety, motor coordination, and locomotor activity have been discussed in various pre-clinical and clinical settings. Several epidemiological and experimental studies have demonstrated the potential effects of ELF-PEMF when exposed >~1h/day; however, very few studies have focused on understanding the influence of ELF-PEMF exposure of 1-3 mT with an exposure duration of <1h/day on spontaneous alternation, anxiety, motor coordination, and locomotor activity. Hence, we attempted to study the effects of ELF-PEMF exposure of 1-3 mT, 50Hz with an exposure duration of 20min each with a 4h gap (2 times) on the cellular proliferation and morphologies of C6 (Glial) cells and spontaneous alternation, anxiety, motor coordination and locomotor activity of Wistar rats under

in vitro and in vivo conditions, respectively. The results showed that ELF-PEMF exposure did not induce any significant levels of cellular fragmentation and changes in the morphology of glial cells. Also, the outcomes revealed no noticeable effects on spontaneous alternation, anxiety, motor coordination, and locomotor activity in PEMF-exposed groups compared with the control. No undesirable side effects were observed at the highest dose (B=3 mT). We also performed histological analysis of the selected brain sections (hippocampus and cortex) following ELF-PEMF exposure. Incidentally, no significant changes were observed in cortical cell counts, tissue structure, and morphology.

(E) Terraneo A, Leggio L, Saladini M, Ermani M, Bonci A, Gallimberti L. Transcranial magnetic stimulation of dorsolateral prefrontal cortex reduces cocaine use: A pilot study. Eur Neuropsychopharmacol. 26:37-44, 2016. (HU, CE, BE, MA)

Recent animal studies demonstrate that compulsive cocaine seeking strongly reduces prelimbic frontal cortex activity, while optogenetic stimulation of this brain area significantly inhibits compulsive cocaine seeking, providing a strong rationale for applying brain stimulation to reduce cocaine consumption. Thus, we employed repetitive transcranial magnetic stimulation (rTMS), to test if dorsolateral prefrontal cortex (DLPFC) stimulation might prevent cocaine use in humans. Thirty-two cocaine-addicted patients were randomly assigned to either the experimental group (rTMS) on the left DLPFC, or to a control group (pharmacological agents) during a 29-day study (Stage 1). This was followed by a 63-day follow-up (Stage 2), during which all participants were offered rTMS treatment. Amongst the patients who completed Stage 1, 16 were in the rTMS group (100%) and 13 in the control group (81%). No significant adverse events were noted. During Stage 1, there were a significantly higher number of cocaine-free urine drug tests in the rTMS group compared to control (p=0.004). Craving for cocaine was also significantly lower in the rTMS group compared to the controls (p=0.038). Out of 13 patients who completed Stage 1 in the control group, 10 patients received rTMS treatment during Stage 2 and showed significant improvement with favorable outcomes becoming comparable to those of the rTMS group. The present preliminary findings support the safety of rTMS in cocaine-addicted patients, and suggest its potential therapeutic role for rTMS-driven PFC stimulation in reducing cocaine use, providing a strong rationale for developing larger placebo-controlled studies.

(E) Teranishi M, Ito M, Huang Z, Nishiyama Y, Masuda A, Mino H, Tachibana M, Inada T, Ohno K. Extremely Low-Frequency Electromagnetic Field (ELF-EMF) Increases Mitochondrial Electron Transport Chain Activities and Ameliorates Depressive Behaviors in Mice. Int J Mol Sci 25(20):11315, 2024. (AS, CE, CC, BE, OX, MA)

Compromised mitochondrial electron transport chain (ETC) activities are associated with depression in humans and rodents. However, the effects of the enhancement of mitochondrial ETC activities on depression remain elusive. We recently reported that an extremely low-frequency electromagnetic field (ELF-EMF) of as low as 10 μT induced hormetic activation of mitochondrial ETC complexes in human/mouse cultured cells and mouse livers. Chronic social defeat stress (CSDS) for 10 consecutive days caused behavioral defects mimicking depression in mice, and using an ELF-EMF for two to six weeks ameliorated them. CSDS variably decreased the mitochondrial ETC proteins in the prefrontal cortex (PFC) in 10 days, which were increased by an ELF-EMF in six weeks. CSDS had no effect on the mitochondrial oxygen consumption

rate in the PFC in 10 days, but using an ELF-EMF for six weeks enhanced it. CSDS inactivated SOD2 by enhancing its acetylation and increased lipid peroxidation in the PFC. In contrast, the ELF-EMF activated the Sirt3-FoxO3a-SOD2 pathway and suppressed lipid peroxidation. Furthermore, CSDS increased markers for mitophagy, which was suppressed by the ELF-EMF in six weeks. The ELF-EMF exerted beneficial hormetic effects on mitochondrial energy production, mitochondrial antioxidation, and mitochondrial dynamics in a mouse model of depression. We envisage that an ELF-EMF is a promising therapeutic option for depression.

Terzi M, Ozberk B, Deniz OG, Kaplan S. The role of electromagnetic fields in neurological disorders. J Chem Neuroanat. 75(Pt B):77-84, 2016. (Review)

In the modern world, people are exposed to electromagnetic fields (EMFs) as part of their daily lives; the important question is "What is the effect of EMFs on human health?" Most previous studies are epidemiological, and we still do not have concrete evidence of EMF pathophysiology. Several factors may lead to chemical, morphological, and electrical alterations in the nervous system in a direct or indirect way. It is reported that non-ionizing EMFs have effects on animals and cells. The changes they bring about in organic systems may cause oxidative stress, which is essential for the neurophysiological process; it is associated with increased oxidization in species, or a reduction in antioxidant defense systems. Severe oxidative stress can cause imbalances in reactive oxygen species, which may trigger neurodegeneration. This review aims to detail these changes. Special attention is paid to the current data regarding EMFs' effects on neurological disease and associated symptoms, such as headache, sleep disturbances, and fatigue.

(E) Todorović D, Kalauzi A, Prolić Z, Jović M, Mutavdzić D. A method for detecting the effect of magnetic field on activity changes of neuronal populations of Morimus funereus (Coleoptera, Cerambycidae). Bioelectromagnetics. 28(3):238-241, 2007. (AC, AS, EE)

Modification of a new method for detecting changes in the activities of neuronal population and the nearest neuron is described. Preliminary measurements of the influence of a static magnetic field (2 mT) on neuronal population activity on eight individuals of an endangered insect species Morimus funereus are included. Five minutes exposure produced both excitatory (5/8) and inhibitory (3/8) effect on the activity of neuronal population of M. funereus antennal lobe. However, when the reversibility of induced effects was quantitatively analyzed, our results showed that they were prevailingly irreversible: (7/8) for the population, (6/8) for the nearest neuron.

(E) Todorović D, Marković T, Prolić Z, Mihajlović S, Rauš S, Nikolić L, Janać B. The influence of static magnetic field (50 mT) on development and motor behaviour of Tenebrio (Insecta, Coleoptera). Int J Radiat Biol. 89(1):44-50, 2013. (AS, CE, DE, BE)

PURPOSE: There is considerable concern about potential effects associated with exposure to magnetic fields on organisms. Therefore, duration of pupa-adult development and motorbehaviour of adults were analyzed in Tenebrio obscursus and Tenebrio molitor after exposure to static magnetic field (50 mT). MATERIAL AND METHODS: The experimental groups were: control (kept 5 m from the magnets), groups which pupae and adults were placed closer to the North pole, or closer to the South pole of magnetic dipole. The pupae were exposed to

the magnetic field until the moment of adult eclosion. The pupa-adult development dynamics were recorded daily. Subsequently, behaviour (distance travelled, average speed and immobility) of adults exposed to the magnetic field was monitored in a circular open field arena. RESULTS: Static magnetic field did not affect pupa-adult developmental dynamic of examined Tenebrio species. Exposure to magnetic field did not significantly change motor behaviour of T. obscurus adults. The changes in the motor behaviour of T. molitor induced by static magnetic field were opposite in two experimental groups developed closer to the North pole or closer to the South pole of magnetic dipole. CONCLUSION: Static magnetic field (50 mT) did not affect on pupa-adult development dynamic of two examined Tenebrio species, but modulated their motor behaviour.

(E) Todorović D, Prolić Z, Petković B, Kalauzi A. Effects of two different waveforms of ELF MFs on bioelectrical activity of antennal lobe neurons of Morimus funereus (Insecta, Coleoptera). Int J Radiat Biol. 91:435-442, 2015. (AS, AE, EE) (waveform)

PURPOSE: External magnetic fields (MFs) interact with organisms at all levels, including the nervous system. Bioelectrical activity of antennal lobe neurons of adult Morimus funereus was analyzed under the influence of extremely low frequency MF (ELF MF, 50 Hz, 2 mT) of different characteristics (exposure duration and waveform). MATERIAL AND METHODS: Neuronal activity (background/neuronal population and those nearest to the recording electrode) in adult longhorn beetles was registered through several phases of exposure to the sine wave and square wave MFs for 5, 10 and 15 min. RESULTS: The sine wave MF, regardless of the exposure duration, did not change the reversibility factor of antennal lobe neuronal activity in adult M. funereus. In contrast, reversibility factors of the nearest neurons were significantly changed after the exposure to square wave MF for 10 and 15 min. CONCLUSION: M. funereus individuals are sensitive to both sine wave and square wave ELF MFs (50 Hz, 2 mT) of different duration, whereby their reactions depend on the characteristics of the applied MF and specificity of each individual.

Tota M, Jonderko L, Witek J, Novickij V, Kulbacka J. Cellular and Molecular Effects of Magnetic Fields. Int J Mol Sci 25(16):8973, 2024. (Review)

Recently, magnetic fields (MFs) have received major attention due to their potential therapeutic applications and biological effects. This review provides a comprehensive analysis of the cellular and molecular impacts of MFs, with a focus on both in vitro and in vivo studies. We investigate the mechanisms by which MFs influence cell behavior, including modifications in gene expression, protein synthesis, and cellular signaling pathways. The interaction of MFs with cellular components such as ion channels, membranes, and the cytoskeleton is analyzed, along with their effects on cellular processes like proliferation, differentiation, and apoptosis. Molecular insights are offered into how MFs modulate oxidative stress and inflammatory responses, which are pivotal in various pathological conditions. Furthermore, we explore the therapeutic potential of MFs in regenerative medicine, cancer treatment, and neurodegenerative diseases. By synthesizing current findings, this article aims to elucidate the complex bioeffects of MFs, thereby facilitating their optimized application in medical and biotechnological fields.

(E) Touitou Y, Selmaoui B, Lambrozo J. Assessment of cortisol secretory pattern in workers chronically exposed to ELF-EMF generated by high voltage transmission lines and substations. Environ Int 161:107103, 2022. (HU, CE, CC)

We investigated the effects of extremely-low frequency electromagnetic fields (ELF-EMFs; 50 Hz) on the secretion of cortisol in 14 men (mean age = 38.0 ± 0.9 years) working in extra-high voltage (EHV) substations. The workers dwelt in houses that were close to substations and high-voltage lines. Thus, they had long histories (1-20 years) of long-yerm exposure to ELF-EMFs. Magnetic field strength was recorded using Emdex dosimeters worn by the volunteers day and night for seven days; the one-week geometric mean ranged from 0.1 to 2.6 µT. Blood samples were taken hourly from 20:00 to 08:00 the next morning. Cortisol concentrations and patterns were compared to age-matched, unexposed control subjects whose exposure level was ten times lower. The comparison of the control group (n = 15) and the groups exposed to fields of 0.1-0.3 µT (n = 5) and > 0.3 µT (n = 9), respectively, revealed a significant effect of field intensity on the cortisol secretory pattern. This study strongly suggests that chronic exposure to ELF-EMFs alters the peak-time serum cortisol levels. Studies are required on the effect of this disruption in high-risk populations such as children, elderly people, and patients with cancer.

(NE) Türközer Z, Güler G, Seyhan N. Effects of exposure to 50 Hz electric field at different strengths on oxidative stress and antioxidant enzyme activities in the brain tissue of guinea pigs. Int J Radiat Biol. 84(7):581-590, 2008. (AS, CE, OX)

PURPOSE: The aim of this study was to evaluate the possible effects of varied exposure to 50 Hz extremely low frequency (ELF) electric field (EF) on the lipid peroxidation levels and antioxidant enzyme activities in the brain homogenates of guinea pigs. Subjects were exposed to 2 kV/m, 2.5 kV/m, 3 kV/m, 3.5 kV/m, 4 kV/m, 4.5 kV/m and 5 kV/m electric fields for three days, 8 h a day in both vertical and horizontal directions. MATERIALS AND METHODS: Malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) activities were measured in order to identify possible alterations in lipid peroxidation levels and antioxidant status due to electric field exposure. Xanthine oxidase (XO), myeloperoxidase (MPO) and adenosine deaminase (ADA) activities were also evaluated in the same samples. RESULTS: Although the study showed several positive but non-significant findings ($p > 0.05$), we did not find significant differences among all of the exposed groups and sham groups in lipid peroxidation levels and enzyme activities ($p > 0.05$) at all strengths and in both directions. Furthermore, the result was the same when the comparison was made between the groups in vertical directions and horizontal directions ($p > 0.05$). CONCLUSION: The present study observed effects of 50 Hz EF exposure on lipid peroxidation levels and antioxidant defense mechanisms but these were not statistically significant at the 95% confidence level. Further research on the effects ELF-EF exposure on lipid peroxidation levels and antioxidant defence mechanisms are warranted.

(E) Urnukhsaikhan E, Cho H, Mishig-Ochir T, Seo YK, Park JK. Pulsed electromagnetic fields promote survival and neuronal differentiation of human BM-MSCs Life Sci. 151:130-138, 2016. (CS, AE, CC, MC)

Pulsed electromagnetic fields (PEMF) are known to affect biological properties such as differentiation, regulation of transcription factor and cell proliferation. However, the cell-protective effect of PEMF exposure is largely unknown. The aim of this study is to understand the mechanisms underlying PEMF-mediated suppression of apoptosis and promotion of survival, including PEMF-induced neuronal differentiation. Treatment of induced human BM-MSCs with PEMF increased the expression of neural markers such as NF-L, NeuroD1 and Tau. Moreover, treatment of induced human BM-MSCs with PEMF greatly decreased cell death in a dose- and time-dependent manner. There is evidence that Akt and Ras are involved in neuronal survival and protection. Activation of Akt and Ras results in the regulation of survival proteins such as Bad and Bcl-xL. Thus, the Akt/Ras signaling pathway may be a desirable target for enhancing cell survival and treatment of neurological disease. Our analyses indicated that PEMF exposure dramatically increased the activity of Akt, Rsk, Creb, Erk, Bcl-xL and Bad via phosphorylation. PEMF-dependent cell protection was reversed by pretreatment with LY294002, a specific inhibitor of phosphatidylinositol 3-kinase (PI3K). Our data suggest that the PI3K/Akt/Bad signaling pathway may be a possible mechanism for the cell-protective effects of PEMF.

(E) Urnukhsaikhan E, Mishig-Ochir T, Kim S-C, Park J-K, Seo Y-K. Neuroprotective Effect of Low Frequency-Pulsed Electromagnetic Fields in Ischemic Stroke. Appl Biochem Biotechnol 181(4):1360-1371, 2017. (AS, CE, CC, MA)

Low frequency-pulsed electromagnetic fields (LF-PEMFs) affect many biological processes; however, the fundamental mechanisms responsible for these effects remain unclear. Our study aimed to investigate the effect of LF-PEMFs on neuroprotection after ischemic stroke. C57B6 mice were exposed to LF-PEMF (F = 60 Hz, Bm = 10 mT) after photothrombotic occlusion. We measured the BDNF/TrkB/Akt signaling pathway, pro-apoptotic and pro-survival protein and gene expressions, and the expression of inflammatory mediators and performed behavioral tests in both LF-PEMF-treated and untreated ischemic stroke mice. Our results showed that LF-PEMF treatment promotes activation of the BDNF/TrkB/Akt signaling pathway. Subsequently, pro-survival proteins were significantly increased, while pro-apoptotic proteins and inflammatory mediators were decreased in ischemic stroke mice after LF-PEMF treatment. The results demonstrated that LF-PEMF exposure has a neuroprotective effect after ischemic stroke in mice during the recovery process.

(NE) van der Mark M, Vermeulen R, Nijssen PC, Mulleners WM, Sas AM, van Laar T, Kromhout H, Huss A. Extremely low-frequency magnetic field exposure, electrical shocks and risk of Parkinson's disease. Int Arch Occup Environ Health. 88(2):227-234, 2015. (HU, ND)

PURPOSE: Previous studies did not provide strong evidence for an increased Parkinson's disease (PD) risk after exposure to extremely low-frequency magnetic fields (ELF-MF), but were limited in their scope to address other exposures related to the use of electricity such as electrical shocks. We evaluated the associations of PD with exposure to ELF-MF, electrical

shocks and having worked in "electrical occupations." **METHODS:** We conducted a hospital-based case-control study, including 444 PD patients and 876 age- and sex-matched controls. Occupational histories were collected in telephone interviews and were linked to job-exposure matrices on ELF-MF exposure and on electrical shocks. In addition, questions on use of household appliances involving ELF-MF exposure, experienced electrical shocks and potential confounders were asked. **RESULTS:** No association of PD risk with any of the evaluated exposures related to electricity was observed. We did, however, observe quite consistently reduced risk estimates across the majority of the exposure categories explored. Given the results of the previous studies and the absence of any postulated mechanism, this is unlikely to represent a true protective effect of ELF-MF or electrical shocks on the occurrence of PD. **CONCLUSIONS:** The results of this study suggest that no association exists between PD and exposure to ELF-MF, electrical shocks or having worked in "electrical occupations."

(E) van Nierop LE, Slottje P, van Zandvoort MJE, de Vocht F, Kromkout H. Effects of magnetic stray fields from a 7 Tesla MRI scanner on neurocognition: a double-blind randomised crossover study. Occup Environ Med 69(10):759-766, 2012. (HU, BE)

Objective: This study characterises neurocognitive domains that are affected by movement-induced time-varying magnetic fields (TVMF) within a static magnetic stray field (SMF) of a 7 Tesla (T) MRI scanner. Methods: Using a double-blind randomised crossover design, 31 healthy volunteers were tested in a sham (0 T), low (0.5 T) and high (1.0 T) SMF exposure condition. Standardised head movements were made before every neurocognitive task to induce TVMF. Results: Of the six tested neurocognitive domains, we demonstrated that attention and concentration were negatively affected when exposed to TVMF within an SMF (varying from 5.0% to 21.1% per Tesla exposure, $p<0.05$), particular in situations were high working memory performance was required. In addition, visuospatial orientation was affected after exposure (46.7% per Tesla exposure, $p=0.05$). Conclusion: Neurocognitive functioning is modulated when exposed to movement-induced TVMF within an SMF of a 7 T MRI scanner. Domains that were affected include attention/concentration and visuospatial orientation. Further studies are needed to better understand the mechanisms and possible practical safety and health implications of these acute neurocognitive effects.

(E) van Nierop LE, Slottje P, van Zandvoort M, Kromhout H. Simultaneous exposure to MRI-related static and low-frequency movement-induced time-varying magnetic fields affects neurocognitive performance: A double-blind randomized crossover study. Magn Reson Med. 74(3):840-849, 2015. (AE, HU, BE)

PURPOSE: This experimental study aims to separate neurocognitive effects resulting from exposure to static magnetic stray fields (SMF) alone and the combination of SMF and low-frequency movement-induced time-varying magnetic fields (TVMF) using a 7 Tesla (T) MRI scanner in stand-by mode. METHODS: In a double-blind randomized crossover experiment, 36 healthy volunteers underwent four sessions, two exposed conditions, and two corresponding sham conditions. The exposure conditions were in front of the scanner bore and consisted of

1.0 T SMF with or without 2.4 T/s TVMF, induced by standardized head movements before each of the five neurocognitive tasks. These specific tasks were selected because previous experiments showed negative effects of SMF + TVMF exposure on test performance. RESULTS: Exposure to SMF in combination with TVMF decreased verbal memory performance significantly and changed visual acuity. Similarly, attention and concentration were negatively affected with borderline significance. Exposure to SMF only did not have significant effects on the performance on any of the tasks. CONCLUSION: Neurocognitive effects were only observed when simultaneously exposed to SMF and TVMF from a 7 T MRI scanner. Therefore, exposure to TVMF seems essential in eliciting the neurocognitive effects in our present study and, presumably, previous experiments.

Vanderstraeten J, Burda H, Verschaeve L, De Brouwer C. Could Magnetic Fields Affect the Circadian Clock Function of Cryptochromes? Testing the Basic Premise of the Cryptochrome Hypothesis (ELF Magnetic Fields). Health Phys. 109(1):84-89, 2015. (opinion)

It has been suggested that weak 50/60 Hz [extremely low frequency (ELF)] magnetic fields (MF) could affect circadian biorhythms by disrupting the clock function of cryptochromes (the "cryptochrome hypothesis," currently under study). That hypothesis is based on the premise that weak (Earth strength) static magnetic fields affect the redox balance of cryptochromes, thus possibly their signaling state as well. An appropriate method for testing this postulate could be real time or short-term study of the circadian clock function of retinal cryptochromes under exposure to the static field intensities that elicit the largest redox changes (maximal "low field" and "high field" effects, respectively) compared to zero field. Positive results might encourage further study of the cryptochrome hypothesis itself. However, they would indicate the need for performing a similar study, this time comparing the effects of only slight intensity changes (low field range) in order to explore the possible role of the proximity of metal structures and furniture as a confounder under the cryptochrome hypothesis.

(E) Varró P, Szemerszky R, Bárdos G, Világi I. Changes in synaptic efficacy and seizure susceptibility in rat brain slices following extremely low-frequency electromagnetic field exposure. Bioelectromagnetics. 30(8):631-640, 2009. (AS, CS, FC)

The effects of electromagnetic fields (EMFs) on living organisms are recently a focus of scientific interest, as they may influence everyday life in several ways. Although the neural effects of EMFs have been subject to a considerable number of investigations, the results are difficult to compare since dissimilar exposure protocols have been applied on different preparations or animals. In the present series of experiments, whole rats or excised rat brain slices were exposed to a reference level-intensity (250-500 microT, 50 Hz) EMF in order to examine the effects on the synaptic efficacy in the central nervous system. Electrophysiological investigation was carried out ex vivo, on neocortical and hippocampal slices; basic synaptic functions, short- and long-term plasticity and seizure susceptibility were tested. The most pronounced effect was a decrease in basic synaptic activity in slices treated directly ex vivo observed as a diminution in amplitude of evoked potentials. On the other hand, following whole-body exposure an

enhanced short- and long-term synaptic facilitation in hippocampal slices and increased seizure susceptibility in neocortical slices was also observed. However, these effects seem to be transient. We can conclude *that* ELF-EMF exposure exerts significant effects on synaptic activity, but the overall changes may strongly depend on the synaptic structure and neuronal network of the affected region together with the specific spatial parameters and constancy of EMF.

(E) Volkow ND, Tomasi D, Wang GJ, Fowler JS, Telang F, Wang R, Alexoff D, Logan J, Wong C, Pradhan K, Caparelli EC, Ma Y, Jayne M. Effects of low-field magnetic stimulation on brain glucose metabolism. Neuroimage. 51(2):623-628, 2010. (HU, AE, FC)

Echo planar imaging (EPI), the gold standard technique for functional MRI (fMRI), is based on fast magnetic field gradient switching. These time-varying magnetic fields induce electric (E) fields in the brain that could influence neuronal activity; but this has not been tested. Here we assessed the effects of EPI on brain glucose metabolism (marker of brain function) using PET and 18F 2-fluoro-2-deoxy-D-glucose ((18)FDG). Fifteen healthy subjects were in a 4 T magnet during the (18)FDG uptake period twice: with (ON) and without (OFF) EPI gradients pulses along the z-axis (G(z): 23 mT/m; 250 mus rise-time; 920 Hz). The E-field from these EPI pulses is non-homogeneous, increasing linearly from the gradient's isocenter (radial and z directions), which allowed us to assess the correlation between local strength of the E-field and the regional metabolic differences between ON and OFF sessions. Metabolic images were normalized to metabolic activity in the plane positioned at the gradient's isocenter where E=0 for both ON and OFF conditions. Statistical parametric analyses used to identify regions that differed between ON versus OFF ($p<0.05$, corrected) showed that the relative metabolism was lower in areas at the poles of the brain (inferior occipital and frontal and superior parietal cortices) for ON than for OFF, which was also documented with individual region of interest analysis. Moreover the magnitude of the metabolic decrements was significantly correlated with the estimated strength of E ($r=0.68$, $p<0.0001$); the stronger the E-field the larger the decreases. However, we did not detect differences between ON versus OFF conditions on mood ratings nor on absolute whole brain metabolism. This data provides preliminary evidence that EPI sequences may affect neuronal activity and merits further investigation.

(E) Walker JL, Kryscio R, Smith J, Pilla A, Sisken BF. Electromagnetic field treatment of nerve crush injury in a rat model: effect of signal configuration on functional recovery. Bioelectromagnetics. 28(4):256-263, 2007. (AS, CE, FC, MA)

Electromagnetic fields (EMFs) have been demonstrated to enhance mammalian peripheral nerve regeneration in vitro and in vivo. Using an EMF signal shown to enhance neurite outgrowth in vitro, we tested this field in vivo using three different amplitudes. The rat sciatic nerve was crushed. Whole body exposure was performed for 4 h/day for 5 days in a 96-turn solenoid coil controlled by a signal generator and power amplifier. The induced electric field at the target tissue consisted of a bipolar rectangular pulse, having 1 and 0.3 ms durations in each polarity, respectively. Pulse repetition rate was 2 per second. By varying the current, the coils produced fields consisting of sham

(no current) and peak magnetic fields of 0.03 mT, 0.3 mT, and 3 mT, corresponding to peak induced electric fields of 1, 10, and 100 microV/cm, respectively, at the tissue target. Walking function was assessed over 43 days using video recording and measurement of the 1-5 toe-spread, using an imaging program. Comparing injured to uninjured hind limbs, mean responses were evaluated using a linear mixed statistical model. There was no difference found in recovery of the toe-spread function between any EMF treatments compared to sham.

(E) Wallace J, Shang W, Gitton C, Hugueville L, Yahia-Cherif L, Selmaoui B. Theta band brainwaves in human resting EEG modulated by mobile phone radiofrequency. Int J Radiat Biol 99(10):1639-1647, 2023. (HU, AE, EE)

Purpose Wireless communication has become an integral part of our lives. The growing number of antennas in our environment and the expanding use of mobile phones (MPs) are increasing the population's exposure to electromagnetic fields. The present study aimed to examine the potential impact of MPs radiofrequency electromagnetic fields (RF-EMF) exposure on the brainwaves of the resting electroencephalogram (EEG) in humans. **Materials and methods:** Twenty-one healthy volunteers were exposed to Global System for Mobile communications (GSM) signal at 900 MHz MP RF-EMF. The maximum specific absorption rate (SAR) of the MP averaged on 10 g tissue and 1 g tissue were measured at 0.49 W/kg, 0.70 W/kg, respectively. **Results:** Results showed that while delta and beta rhythms of resting EEG were not affected, theta brainwaves were significantly modulated during exposure to RF-EMF related to MPs. For the first time, it was shown that this modulation is dependent on the eye condition, i.e., closed or open. **Conclusions:** This study strongly suggests that acute exposure to RF-EMF alters the EEG theta rhythm at rest. Long-term exposure studies are required to explore the effect of this disruption in high-risk or sensitive populations.

(E) Wang CX, Hilburn IA, Wu DA , Mizuhara Y, Cousté CP, Abrahams JNH, Bernstein SE, Matani A, Shimojo S, Kirschvink JL. Transduction of the Geomagnetic Field as Evidenced from alpha-Band Activity in the Human Brain. eNeuro. 6(2). pii: ENEURO.0483-18.2019. (HU, AE, EE)

Magnetoreception, the perception of the geomagnetic field, is a sensory modality well-established across all major groups of vertebrates and some invertebrates, but its presence in humans has been tested rarely, yielding inconclusive results. We report here a strong, specific human brain response to ecologically-relevant rotations of Earth-strength magnetic fields. Following geomagnetic stimulation, a drop in amplitude of electroencephalography (EEG) alpha-oscillations (8-13 Hz) occurred in a repeatable manner. Termed alpha-event-related desynchronization (alpha-ERD), such a response has been associated previously with sensory and cognitive processing of external stimuli including vision, auditory and somatosensory cues. Alpha-ERD in response to the geomagnetic field was triggered only by horizontal rotations when the static vertical magnetic field was directed downwards, as it is in the Northern Hemisphere; no brain responses were elicited by the same horizontal rotations when the static vertical component was directed upwards. This implicates a biological response tuned to the ecology of the local human population, rather than a generic physical effect. Biophysical tests showed that the neural response was sensitive to static components of the

magnetic field. This rules out all forms of electrical induction (including artifacts from the electrodes) which are determined solely on dynamic components of the field. The neural response was also sensitive to the polarity of the magnetic field. This rules out free-radical "quantum compass" mechanisms like the cryptochrome hypothesis, which can detect only axial alignment. Ferromagnetism remains a viable biophysical mechanism for sensory transduction and provides a basis to start the behavioral exploration of human magnetoreception.

(E) Wang K, Wang H, Dong J, Zhao L, Wang H, Zhang J, Xu X, Yao B, Lai Y, Peng R. Alterations in the Temporal Variation and Spatial Distribution of Blood-Brain Barrier Permeability Following Electromagnetic Pulse Radiation: A Study Based on Dynamic Contrast-Enhanced MRI. Brain Sci. 15(6):577, 2025. (AS, AE, MC, MA, EF)

Background: Previous studies have suggested that electromagnetic pulse (EMP) can induce openings in the blood-brain barrier (BBB). However, the temporal variation and spatial distribution of BBB permeability after EMP radiation are difficult to assess using conventional histopathological approaches. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a valuable tool for the in vivo evaluation of BBB permeability. The main purpose of this study was to investigate the temporal variation and spatial distribution of BBB permeability after EMP radiation in rats using DCE-MRI. **Methods:** The dose of EMP was estimated through simulations utilizing a digital rat model comprising 16 distinct brain regions. Then, the changes in BBB permeability of the different rat brain regions at different time points (3 h and 24 h) after EMP radiation were evaluated using quantitative DCE-MRI. Furthermore, the spatial difference in BBB permeability was assessed 3 h after exposure. Finally, the dose-effect relationship between the electric field strength and the BBB permeability was also investigated. **Results:** The results demonstrated that the changes in the values of volume transfer constant (ΔK^{trans}) significantly increased in several rat brain regions at 3 h after 400 kV/m EMP radiation. These changes vanished 24 h after exposure. Meanwhile, no significant spatial differences in BBB permeability were observed after EMP radiation. Moreover, Pearson's correlation analysis showed that there was a significant positive linear relationship between BBB permeability and the electric field strength within an external electric field strength range of 0 to 400 kV/m at 3 h after EMP radiation. **Conclusions:** EMP radiation can induce a reversible increase in BBB permeability in rats. Moreover, no significant differences in BBB permeability were found across different brain regions. Additionally, the degree of BBB permeability was positively correlated with the regional electric field strength of EMP radiation within an external electric field strength range of 0 to 400 kV/m at 3 h after EMP radiation. These results indicate the promising potential of employing EMP for transient openings in the BBB, which could facilitate clinical pharmacological interventions via drug delivery into the brain.

(E) Wang L, Yang J, Wang F, Zhou P, Wang K, Ming D. Modulation of Low-Frequency Pulsed Magnetic Field on Hippocampal Neural Oscillation in Depression Rats. Annu Int Conf IEEE Eng Med Biol Soc 2018:259-262, 2018. (AS. LE. BE, EE, MA)

Transcranial magnetic stimulation (TMS), as a non-invasive brain stimulation technique, has been approved for some medication-resistant depression by the United States Food and Drug

Administration. However, the majority of these studies have focused on the effects of high-frequency TMS, and little is known about low-frequency TMS in depression treatment. Furthermore, the potential electroneurophysiology mechanisms of TMS on the improvement of and function of the brain remain poorly understood. In the present study, a depression rat model was established by chronic unpredictable stress (CUS). Rats were exposed to low-frequency pulsed magnetic field (LFPMF) (1Hz, 20mT) for 14 days, one hour per day, then elevated plus-maze test was assessed and local field potentials (LFPs) in hippocampus were recorded. In order to analyze LFPs, sample entropy was calculated to make complexity analysis, while phase locked value and phase-amplitude coupling modulation index were used to figure out the correlation of oscillations. Our data showed that LFPMF significantly relieved CUS-induced depression-behaviors and improved the undesirable changes of the identical-frequency synchronization and theta-gamma phase-amplitude coupling in CUS rats. These findings indicated that the antidepressive-like effects of LFPMF might be associated with the LFPMF-induced improvement in neural oscillation.

(E) Wang L, Li S, Li T, Zheng W, Li Y, Xu G. [Effects of 50 Hz electromagnetic field on rat working memory and investigation of neural mechanisms] Sheng Wu Yi Xue Gong Cheng Xue Za Zhi 40(6):1135-1141, 2023. [Article in Chinese] (AS, CE, EE, BE)

With the widespread use of electrical equipment, cognitive functions such as working memory (WM) could be severely affected when people are exposed to 50 Hz electromagnetic fields (EMF) for long term. However, the effects of EMF exposure on WM and its neural mechanism remain unclear. In the present paper, 15 rats were randomly assigned to three groups, and exposed to an EMF environment at 50 Hz and 2 mT for a different duration: 0 days (control group), 24 days (experimental group I), and 48 days (experimental group II). Then, their WM function was assessed by the T-maze task. Besides, their local field potential (LFP) in the media prefrontal cortex (mPFC) was recorded by the *in vivo* multichannel electrophysiological recording system to study the power spectral density (PSD) of θ and γ oscillations and the phase-amplitude coupling (PAC) intensity of θ-γ oscillations during the T-maze task. The results showed that the PSD of θ and γ oscillations decreased in experimental groups I and II, and the PAC intensity between θ and high-frequency γ (hγ) decreased significantly compared to the control group. The number of days needed to meet the task criterion was more in experimental groups I and II than that of control group. The results indicate that long-term exposure to EMF could impair WM function. The possible reason may be the impaired communication between different rhythmic oscillations caused by a decrease in θ-hγ PAC intensity. This paper demonstrates the negative effects of EMF on WM and reveals the potential neural mechanisms from the changes of PAC intensity, which provides important support for further investigation of the biological effects of EMF and its mechanisms.

(E) Wang S, Mao S, Yao B, Xiang D, Fang C. Effects of low-frequency repetitive transcranial magnetic stimulation on depression- and anxiety-like behaviors in epileptic rats. J Integr Neurosci 18(3):237-243, 2019. (AS, CE, BE, MA)

Low-frequency repetitive transcranial magnetic stimulation (rTMS) has been considered as a treatment option for depression and anxiety. However, its role in epilepsy comorbid with depression and anxiety is unclear. Therefore, we evaluated whether low-frequency rTMS can

alleviate depression- and anxiety-like behavior in epileptic rats. Forty-eight adult rats were allocated at random to four groups: Control, Pentylenetetrazol (PTZ), PTZ-rTMS and PTZ-Sham. The control group received intraperitoneal injections of normal saline, while the other groups received intraperitoneal injections of pentylenetetrazol (35 mg/kg/d) once a day for 15 days. Low-frequency rTMS or sham stimulation were administered to the PTZ-rTMS and PTZ-Sham group, respectively, over the two-week period. The open-field test (OFT), elevated plus-maze test (EPM) and forced swimming test (FST) were carried out before the experiment, on the 8th and 15th day to assess depression- and anxiety-like behavior in the rats. Two weeks of low-frequency rTMS treatment could not impair the increases of seizure severity in epileptic rats. However, relative to the PTZ and PTZ-Sham group, the two-week low-frequency rTMS treatment significantly reduced the immobility time in the forced swimming test and attenuated the progressive decrease in total distance traveled, frequency of rearing, velocity in the open-field test, number of entries in the open arms (%) and the time spent in the open arms (%) in the elevated plus-maze test of the PTZ-rTMS group. We proposed that low-frequency rTMS can benefit epileptic rats via amelioration of comorbid depression and anxiety, but it can not alleviate the seizure severity.

(E) Wang X, Liu Y, Lei Y, Zhou D, Fu Y, Che Y, Xu R, Yu H, Hu X, Ma Y. Extremely low-frequency electromagnetic field exposure during chronic morphine treatment strengthens downregulation of dopamine D2 receptors in rat dorsal hippocampus after morphine withdrawal. Neurosci Lett. 433(3):178-82, 2008. (AS, CE, CC)

The aim of this study was to investigate the effect of extremely low-frequency electromagnetic field (ELF-EMF) exposure during morphine treatment on dopamine D2 receptor (D2R) density in the rat dorsal hippocampus following withdrawal. Rats were exposed to ELF-EMF (20 Hz, 14 mT) or sham exposed for 1h per day before injection of morphine (10mg/kg, i.p.) once daily for 12 days. The saline control group was sham exposed for the same period. Immunohistochemistry was used to detect the density of D2Rs on the 1st, 3rd and 5th morphine withdrawal days. The results showed that the density of D2Rs in sham-exposed morphine-treated rats on the 1st and 3rd days of morphine withdrawal was significantly lower than that of the saline control group. The ELF-EMF-exposed morphine group also exhibited a significantly lower density of D2Rs on the 1st and 3rd withdrawal days relative to the sham-exposed morphine group. However, the D2R density in both groups tended to recover as morphine withdrawal days increased. The results suggest that dorsal hippocampal D2Rs are sensitive to morphine withdrawal and that this is potentiated by ELF-EMF pre-exposure during morphine treatment.

(E) Wang X, Zhao K, Wang D, Adams W, Fu Y, Sun H, Liu X, Yu H, Ma Y. Effects of exposure to a 50 Hz sinusoidal magnetic field during the early adolescent period on spatial memory in mice. Bioelectromagnetics. 34(4):275-284, 2013. (AS, CE, BE)

Adolescence is a critical developmental stage during which substantial remodeling occurs in brain areas involved in emotional and learning processes. Although a robust literature on the biological effects of extremely low frequency magnetic fields (ELF-MFs) has been documented,

data on the effects of ELF-MF exposure during this period on cognitive functions remain scarce. In this study, early adolescent male mice were exposed from postnatal day (P) 23-35 to a 50 Hz MF at 2 mT for 60 min/day. On P36-45, the potential effects of the MF exposure on spatial memory performance were examined using the Y-maze and Morris water maze tasks. The results showed that the MF exposure did not affect Y-maze performance but improved spatial learning acquisition and memory retention in the water maze task under the present experimental conditions.

Wang X, Ye Y, Zuo H, Li Y. Neurobiological effects and mechanisms of magnetic fields: a review from 2000 to 2023. BMC Public Health 24(1):3094, 2024. (Review)

Magnetic fields are widely used in medical diagnostics because of their superior non-invasive properties. In addition, with the widespread use of magnetic fields in transportation and other areas, their potential hazards to human health and the assessment of their safety have attracted considerable attention. The effects of magnetic fields on living organisms have a long history. The biological effects of magnetic field exposure in mice and rats depend on the magnetic field strength, exposure time, and direction; depending on these and potentially other factors, magnetic fields can cause a series of neurobiological effects. We reviewed global research on the neurobiological effects of magnetic fields from recent years to provide an overview and insights into the underlying mechanisms. This review focuses on the biological effects of static and dynamic magnetic fields of different frequencies and intensities on animals and nerve cells and their mechanisms of action.

(E) Wang Y, Feng L, Liu S, Zhou X, Yin T, Liu Z, Yang Z . Transcranial Magneto-Acoustic Stimulation Improves Neuroplasticity in Hippocampus of Parkinson's Disease Model Mice. Neurotherapeutics 16(4):1210-1224, 2019. .(VO, CE, BE, CC, MA)

In this study, we have, for the first time, demonstrated the beneficial effects of transcranial magneto-acoustic stimulation (TMAS), a technique based on focused ultrasound stimulation within static magnetic field, on the learning and memory abilities and neuroplasticity of the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mouse model of Parkinson's disease (PD). Our results showed that chronic TMAS treatment (2 weeks) improved the outcome of Morris water maze, long-term potentiation (LTP), and dendritic spine densities in the dentate gyrus (DG) region of the hippocampus of PD model mice. To further investigate into the underlying mechanisms of these beneficial effects by TMAS, we quantified the proteins in the hippocampus that regulated neuroplasticity. Results showed that the level of postsynaptic density protein 95 was elevated in the brain of TMAS-treated PD model mice while the level of synaptophysin (SYP) did not show any change. We further quantified proteins that mediated neuroplasticity mechanisms, such as brain-derived neurotrophic factor (BDNF) and other important proteins that mediated neuroplasticity. Results showed that TMAS treatment elevated the levels of BDNF, cAMP response element-binding protein (CREB), and protein kinase B (p-Akt) in the PD model mouse hippocampus, but not in the non-PD mouse hippocampus. These results suggest that the beneficial effects on the neuroplasticity of PD model mice treated with TMAS could possibly be conducted through postsynaptic regulations and mediated by BDNF.

(E) Wang Z, Che PL, Du J, Ha B, Yarema KJ. Static magnetic field exposure reproduces cellular effects of the Parkinson's disease drug candidate ZM241385. PLoS One. 5(11):e13883, 2010. (AE, CS, CC, ND, MA)

BACKGROUND: This study was inspired by coalescing evidence that magnetic therapy may be a viable treatment option for certain diseases. This premise is based on the ability of moderate strength fields (i.e., 0.1 to 1 Tesla) to alter the biophysical properties of lipid bilayers and in turn modulate cellular signaling pathways. In particular, previous results from our laboratory (Wang et al., BMC Genomics, 10, 356 (2009)) established that moderate strength static magnetic field (SMF) exposure altered cellular endpoints associated with neuronal function and differentiation. Building on this background, the current paper investigated SMF by focusing on the adenosine A(2A) receptor (A(2A)R) in the PC12 rat adrenal pheochromocytoma cell line that displays metabolic features of Parkinson's disease (PD). **METHODOLOGY AND PRINCIPAL FINDINGS:** SMF reproduced several responses elicited by ZM241385, a selective A(2A)R antagonist, in PC12 cells including altered calcium flux, increased ATP levels, reduced cAMP levels, reduced nitric oxide production, reduced p44/42 MAPK phosphorylation, inhibited proliferation, and reduced iron uptake. SMF also counteracted several PD-relevant endpoints exacerbated by A(2A)R agonist CGS21680 in a manner similar to ZM241385; these include reduction of increased expression of A(2A)R, reversal of altered calcium efflux, dampening of increased adenosine production, reduction of enhanced proliferation and associated p44/42 MAPK phosphorylation, and inhibition of neurite outgrowth. **CONCLUSIONS AND SIGNIFICANCE:** When measured against multiple endpoints, SMF elicited qualitatively similar responses as ZM241385, a PD drug candidate. Provided that the in vitro results presented in this paper apply in vivo, SMF holds promise as an intriguing non-invasive approach to treat PD and potentially other neurological disorders.

(E) Weerasinghe AM, Liyanage S, Kawshalya MADR, Hong SC. Impact of exposure to extremely low-frequency magnetic fields on blood pressure, heart rate variation and disturbance to quality of sleep on industrial workers in Korea. Int J Occup Saf Ergon 2024 Nov 23:1-8. doi: 10.1080/10803548.2024.2413816. Online ahead of print. (CE, HU, BE, FC)

Objectives: This study investigates the potential health risks associated with exposure to extremely low-frequency magnetic fields (ELF-MFs), focusing on the impact on sleep quality. The hypothesis is that increasing ELF-MF exposure will correlate with elevated blood pressure (BP), altered heart rate (HR) dynamics and poorer sleep quality among occupational workers in Korea.**Methods:** The study involved 85 participants. Assessment of ELF-MF exposure was carried out continuously for 24 h in the two groups. Measurements of BP parameters, HR and sleep quality were conducted accordingly.**Results:** The study found significant ELF-MF exposure levels in both working and sleeping times for industrial factory workers (0.19 ± 0.38 and 0.17 ± 0.23 μT, $p < 0.05$). Long-term exposure among industrial workers may contribute to a significant difference in systolic blood pressure (SBP) (125.61 ± 9.60 mm Hg, $p < 0.05$). Additionally, a significant difference in deep sleep analysis was observed between the high-exposure and low-exposure groups (67.13 ± 31.15 min, $p < 0.05$). **Conclusion:** The hypothesis

was confirmed, indicating possible effects of high ELF-MF exposure on SBP and deep sleep. However, further research on long-term exposure and its association with sleep quality disturbances is needed for validation.

(E) Wu CL, Fu TF, Chiang MH, Chang YW, Her JL, Wu T. Magnetoreception Regulates Male Courtship Activity in Drosophila. PLoS One. 11(5):e0155942, 2016. (AS, CE, BE)

The possible neurological and biophysical effects of magnetic fields on animals is an area of active study. Here, we report that courtship activity of male Drosophila increases in a magnetic field and that this effect is regulated by the blue light-dependent photoreceptor cryptochrome (CRY). Naïve male flies exhibited significantly increased courtship activities when they were exposed to a ≥ 20-Gauss static magnetic field, compared with their behavior in the natural environment (0 Gauss). CRY-deficient flies, cryb and crym, did not show an increased courtship index in a magnetic field. RNAi-mediated knockdown of cry in cry-GAL4-positive neurons disrupted the increased male courtship activity in a magnetic field. Genetically expressing cry under the control of cry-GAL4 in the CRY-deficient flies restored the increase in male courtship index that occurred in a magnetic field. Interestingly, artificially activating cry-GAL4-expressing neurons, which include large ventral lateral neurons and small ventral lateral neurons, via expression of thermosensitive cation channel dTrpA1, also increased the male courtship index. This enhancement was abolished by the addition of the cry-GAL80 transgene. Our results highlight the phenomenon of increased male courtship activity caused by a magnetic field through CRY-dependent magnetic sensation in CRY expression neurons in Drosophila.

(E) Wyszkowska J, Shepherd S, Sharkh S, Jackson CW, Newland PL. Exposure to extremely low frequency electromagnetic fields alters the behaviour, physiology and stress protein levels of desert locusts. Sci Rep. 6:36413, 2016. (AS, AE, BE, CC, EE)

Electromagnetic fields (EMFs) are present throughout the modern world and are derived from many man-made sources including overhead transmission lines. The risks of extremely-low frequency (ELF) electromagnetic fields are particularly poorly understood especially at high field strengths as they are rarely encountered at ground level. Flying insects, however, can approach close to high field strength transmission lines prompting the question as to how these high levels of exposure affect behaviour and physiology. Here we utilise the accessible nervous system of the locust to ask how exposure to high levels of ELF EMF impact at multiple levels. We show that exposure to ELF EMFs above 4 mT leads to reduced walking. Moreover, intracellular recordings from an identified motor neuron, the fast extensor tibiae motor neuron, show increased spike latency and a broadening of its spike in exposed animals. In addition, hind leg kick force, produced by stimulating the extensor tibiae muscle, was reduced following exposure, while stress-protein levels (Hsp70) increased. Together these results suggest that ELF EMF exposure has the capacity to cause dramatic effects from behaviour to

physiology and protein expression, and this study lays the foundation to explore the ecological significance of these effects in other flying insects.

(E) Wyszkowska J, Kobak J, Aonuma H. Electromagnetic field exposure affects the calling song, phonotaxis, and level of biogenic amines in crickets. Environ Sci Pollut Res Int. 30(40):93255-93268, 2023. (AS, AE, CC, BE)

The electromagnetic field (EMF) is ubiquitous in the environment, constituting a well-known but poorly understood stressor. Few studies have been conducted on insect responses to EMF, although they are an excellent experimental model and are of great ecological importance. In our work, we tested the effects of EMF (50 Hz, 7 mT) on the cricket Gryllus bimaculatus: the male calling song pattern, female mate choice, and levels of biogenic amines in the brain. Exposure of males to EMF increased the number and shortened the period of chips in their calling song (by 2.7% and 5% relative to the control song, respectively), but not the sound frequency. Aged (3-week-old) females were attracted to both natural and EMF-modified male signals, whereas young (1-week-old, virgin) females responded only to the modified signal, suggesting its higher attractance. Stress response of males to EMF may be responsible for the change in the calling song, as suggested by the changes in the amine levels in their brains: an increase in dopamine (by 50% relative to the control value), tyramine (65%), and serotonin (25%) concentration and a decrease in octopamine level (by 25%). These findings indicate that G. bimaculatus responds to EMF, like stressful conditions, which may change the condition and fitness of exposed individuals, disrupt mate selection, and, in consequence, affect the species' existence.

(E) Xia P, Zheng Y, Dong L, Tian C. Short-Term Extremely Low-Frequency Electromagnetic Field Inhibits Synaptic Plasticity of Schaffer Collateral-CA1 Synapses in Rat Hippocampus via the Ca^{2+}/Calcineurin Pathway. ACS Chem Neurosci 12(19):3550-3557, 2021. (CS, AE, EE)

In this study, we investigate the intrinsic mechanism by which an extremely low-frequency electromagnetic field (ELF-EMF) influences neurons in the Schaffer collateral-CA1 (SC-CA1) region of rat hippocampus using electrophysiological techniques. ELF-EMF has an interesting effect on synaptic plasticity: it weakens long-term potentiation and enhances long-term depression. Here, the magnetic field effect disappeared after a blockade of voltage-gated calcium channels and calcineurin, which are key components in the Ca^{2+}/calcineurin pathway, with two blockers, cadmium chloride and cyclosporin A. This fully establishes that the effect of ELF-EMF on synaptic plasticity is mediated by the Ca^{2+}/calcineurin pathway and represents a novel technique for studying the specific mechanisms of action of ELF-EMF on learning and memory.

(E) Xiong J, He C, Li C, Tan G, Li J, Yu Z, Hu Z, Chen F. Changes of dendritic spine density and morphology in the superficial layers of the medial entorhinal cortex induced by extremely low-frequency magnetic field exposure. PLoS One. 8(12):e83561, 2013. (AS, CE, MC)

In the present study, we investigated the effects of chronic exposure (14 and 28 days) to a 0.5 mT 50 Hz extremely low-frequency magnetic field (ELM) on the dendritic spine density and shape in the superficial layers of the medial entorhinal cortex (MEC). We performed Golgi

staining to reveal the dendritic spines of the principal neurons in rats. The results showed that ELM exposure induced a decrease in the spine density in the dendrites of stellate neurons and the basal dendrites of pyramidal neurons at both 14 days and 28 days, which was largely due to the loss of the thin and branched spines. The alteration in the density of mushroom and stubby spines post ELM exposure was cell-type specific. For the stellate neurons, ELM exposure slightly increased the density of stubby spines at 28 days, while it did not affect the density of mushroom spines at the same time. In the basal dendrites of pyramidal neurons, we observed a significant decrease in the mushroom spine density only at the later time point post ELM exposure, while the stubby spine density was reduced at 14 days and partially restored at 28 days post ELM exposure. ELM exposure-induced reduction in the spine density in the apical dendrites of pyramidal neurons was only observed at 28 days, reflecting the distinct vulnerability of spines in the apical and basal dendrites. Considering the changes in spine number and shape are involved in synaptic plasticity and the MEC is a part of neural network that is closely related to learning and memory, these findings may be helpful for explaining the ELM exposure-induced impairment in cognitive functions.

(E)Xu P, Wang B, Wang Z, Jin R, Ahmad M, Shang Y, Hu M, Chen F, Khalil MF, Hu ang W, Wang Y. Effects of electromagnetic radiation from offshore wind power on the physiology and behavior of two marine fishes. Mar Pollut Bull 213:117633, 2025. (AS, CE, BE, OX)

With the widespread promotion of wind power, its potential ecological impacts on marine ecosystems have raised concerns, among which electromagnetic radiation is one of the significant impacts. It is well known that the effects of electromagnetic fields on different marine organisms vary greatly, but little is known about their effects on commercially important fish species. We studied the toxicity differences between the large yellow croaker (Larimichthys crocea) and the black sea bream (Acanthopagrus schlegelii) when exposed to magnetic field strengths of 0mT, 0.5mT, 1.0mT, 1.5mT and 2.0mT. We found that under the 1.5mT and 2.0mT, the swimming velocity of L. crocea and A. schlegelii was reduced and the antioxidant enzymes in the body had a protective function on the body. Under the 2.0mT, the stress response of A. schlegelii was higher and the immune systems of both fish species were activated. The electromagnetic intensity below 2.0mT was more sensitive to L. crocea and A. schlegelii. However, electromagnetic radiation seems to have no significant effect on the nutrient absorption capacity of the organisms. After several days of recovery, all affected markers showed signs of reversibility. In summary, the experiment could provide valuable data for developing early warning systems and preventive measures to mitigate potential threats to marine life from offshore wind farms.

(E) Xu Y, Gu X, Di G Duration-dependent effect of exposure to static electric field on learning and memory ability in mice. Environ Sci Pollut Res Int 25(24):23864-23874, 2018. (AS, CE, BE)

With the rapid development of ultra-high-voltage direct-current (UHVDC) transmission, the strength of environmental static electric field (SEF) around UHVDC transmission lines increased substantially, which has aroused widely public attention on the potential health effects of SEF. In

this study, the effect of SEF exposure on learning and memory ability was investigated. Institute of Cancer Research mice were exposed to 56.3 kV/m SEF for a short term (7 days) or long term (49 days). Behaviors in the Morris water maze (MWM) test, hippocampal neurotransmitter contents, and oxidative stress indicators were examined. Results showed that short-term SEF exposure significantly prolonged escape latency and decreased the number of platform-site crossovers, as well as decreased the time spent in the target quadrant in the MWM test. Meanwhile, serotonin level and the ratio of glutamate level to γ-aminobutyric acid level changed significantly. Besides, malondialdehyde content and glutathione peroxidase activity increased significantly, while superoxide dismutase activity decreased significantly. After long-term SEF exposure, all indices above showed no significant differences between the SEF and sham exposure groups. These data indicated that short-term exposure to 56.3 kV/m SEF could cause abnormal neurotransmitter levels and oxidative stress in the hippocampus, which led to the decline in learning and memory ability. Under the condition of long-term exposure, the SEF-induced disturbances in neurotransmitter contents and redox balance were offset by the compensatory responses of mice, and thus, the learning and memory ability returned to normal level. The temporary and reversible decline in learning and memory ability was only a common biological effect of SEF rather than a health hazard.

(E) Yakir-Blumkin MB, Loboda Y, Schächter L, Finberg JPM Static Magnetic Field Exposure In Vivo Enhances the Generation of New Doublecortin-expressing Cells in the Sub-ventricular Zone and Neocortex of Adult Rats. Neuroscience 425:217-234, 2020. (AS, CS, CE, MC)

Static magnetic field (SMF) is gaining interest as a potential technique for modulating CNS neuronal activity. Previous studies have shown a pro-neurogenic effect of short periods of extremely low frequency pulsatile magnetic fields (PMF) in vivo and pro-survival effect of low intensity SMF in cultured neurons in vitro, but little is known about the in vivo effects of low to moderate intensity SMF on brain functions. We investigated the effect of continuously-applied SMF on subventricular zone (SVZ) neurogenesis and immature doublecortin (DCX)-expressing cells in the neocortex of young adult rats and in primary cultures of cortical neurons in vitro. A small (3 mm diameter) magnetic disc was implanted on the skull of rats at bregma, producing an average field strength of 4.3 mT at SVZ and 12.9 mT at inner neocortex. Levels of proliferation of SVZ stem cells were determined by 5-ethynyl-2'-deoxyuridine (EdU) labelling, and early neuronal phenotype development was determined by expression of doublecortin (DCX). To determine the effect of SMF on neurogenesis in vitro, permanent magnets were placed beneath the culture dishes. We found that low intensity SMF exposure enhances cell proliferation in SVZ and new DCX-expressing cells in neocortical regions of young adult rats. In primary cortical neuronal cultures, SMF exposure increased the expression of newly generated cells co-labelled with EdU and DCX or the mature neuronal marker NeuN, while activating a set of pro neuronal bHLH genes. SMF exposure has potential for treatment of neurodegenerative disease and conditions such as CNS trauma and affective disorders in which increased neurogenesis is desirable.

(E) Yang G, Ren Z, Mei YA. Exposure to 50 Hz magnetic field modulates $GABA_A$ currents in cerebellar granule neurons through an EP receptor-mediated PKC pathway. J Cell Mol Med. 19(10):2413-2422, 2015. (CS, AE, FC, CC)

Previous work from both our lab and others have indicated that exposure to 50 Hz magnetic fields (ELF-MF) was able to modify ion channel functions. However, very few studies have investigated the effects of MF on γ-aminobutyric acid (GABA) type A receptors ($GABA_A$ Rs) channel functioning, which are fundamental to overall neuronal excitability. Here, our major goal is to reveal the potential effects of ELF-MF on $GABA_A$ Rs activity in rat cerebellar granule neurons (CGNs). Our results indicated that exposing CGNs to 1 mT ELF-MF for 60 min. significantly increased $GABA_A$ R currents without modifying sensitivity to GABA. However, activation of PKA by db-cAMP failed to do so, but led to a slight decrease instead. On the other hand, PKC activation or inhibition by PMA or Bis and Docosahexaenoic acid (DHA) mimicked or eliminated the field-induced-increase of $GABA_A$ R currents. Western blot analysis indicated that the intracellular levels of phosphorylated PKC (pPKC) were significantly elevated after 60 min. of ELF-MF exposure, which was subsequently blocked by application of DHA or EP1 receptor-specific (prostaglandin E receptor 1) antagonist (SC19220), but not by EP2-EP4 receptor-specific antagonists. SC19220 also significantly inhibited the ELF-MF-induced elevation on $GABA_A$ R currents. Together, these data obviously demonstrated for the first time that neuronal $GABA_A$ currents are significantly increased by ELF-MF exposure, and also suggest that these effects are mediated via an EP1 receptor-mediated PKC pathway. Future work will focus on a more comprehensive analysis of the physiological and/or pathological consequences of these effects.

(E) Yi G, Wang J, Wei X, Deng B, Tsang KM, Chan WL, Han C. Effects of extremely low-frequency magnetic fields on the response of a conductance-based neuron model. Int J Neural Syst. 24(1):1450007, 2014. (CS, AE, EE)

To provide insights into the modulation of neuronal activity by extremely low-frequency (ELF) magnetic field (MF), we present a conductance-based neuron model and introduce ELF sinusoidal MF as an additive voltage input. By analyzing spike times and spiking frequency, it is observed that neuron with distinct spiking patterns exhibits different response properties in the presence of MF exposure. For tonic spiking neuron, the perturbations of MF exposure on spike times is maximized at the harmonics of neuronal intrinsic spiking frequency, while it is maximized at the harmonics of bursting frequency for burst spiking neuron. As MF intensity increases, the perturbations also increase. Compared with tonic spiking, bursting dynamics are less sensitive to the perturbations of ELF MF exposure. Further, ELF MF exposure is more prone to perturb neuronal spike times relative to spiking frequency. Our finding suggests that the resonance may be one of the neural mechanisms underlying the modulatory effects of the low-intensity ELF MFs on neuronal activities. The results highlight the impacts of ELF MFs exposure on neuronal activity from the single cell level, and demonstrate various factors including ELF MF properties and neuronal spiking characteristics could determine the outcome of exposure. These insights into the mechanism of MF exposure may be relevant for the design of multi-intensity magnetic stimulus protocols, and may even contribute to the interpretation of MF effects on the central nervous systems.

(E) Yin C, Luo X, Duan Y, Duan W, Zhang H, He Y, Sun G, Sun X. Neuroprotective effects of lotus seedpod procyanidins on extremely low frequency

electromagnetic field-induced neurotoxicity in primary cultured hippocampal neurons. Biomed Pharmacother. 82:628-639, 2016. (CS, AE, OX, MA)

The present study investigated the protective effects of lotus seedpod procyanidins (LSPCs) on extremely low frequency electromagnetic field (ELF-EMF)-induced neurotoxicity in primary cultured rat hippocampal neurons and the underlying molecular mechanism. The results of MTT, morphological observation, superoxide dismutase (SOD) and malondialdehyde (MDA) assays showed that compared with control, incubating neurons under ELF-EMF exposure significantly decreased cell viability and increased the number of apoptotic cells, whereas LSPCs evidently protected the hippocampal neurons against ELF-EMF-induced cell damage. Moreover, a certain concentration of LSPCs inhibited the elevation of intracellular reactive oxygen species (ROS) and Ca(2+) level, as well as prevented the disruption of mitochondrial membrane potential induced by ELF-EMF exposure. In addition, supplementation with LSPCs could alleviate DNA damage, block cell cycle arrest at S phase, and inhibit apoptosis and necrosis of hippocampal neurons under ELF-EMF exposure. Further study demonstrated that LSPCs up-regulated the activations of Bcl-2, Bcl-xl proteins and suppressed the expressions of Bad, Bax proteins caused by ELF-EMF exposure. In conclusion, these findings revealed that LSPCs protected against ELF-EMF-induced neurotoxicity through inhibiting oxidative stress and mitochondrial apoptotic pathway.

(E) Zeng Y, Shen Y , Hong L, Chen Y, Shi X, Zeng Q, Yu P. Effects of Single and Repeated Exposure to a 50-Hz 2-mT Electromagnetic Field on Primary Cultured Hippocampal Neurons. Neurosci Bull. 33(3):299-306, 2017. (CS, AE, CE, OX, FC)

The prevalence of domestic and industrial electrical appliances has raised concerns about the health risk of extremely low-frequency magnetic fields (ELF-MFs). At present, the effects of ELF-MFs on the central nervous system are still highly controversial, and few studies have investigated its effects on cultured neurons. Here, we evaluated the biological effects of different patterns of ELF-MF exposure on primary cultured hippocampal neurons in terms of viability, apoptosis, genomic instability, and oxidative stress. The results showed that repeated exposure to 50-Hz 2-mT ELF-MF for 8 h per day after different times in culture decreased the viability and increased the production of intracellular reactive oxidative species in hippocampal neurons. The mechanism was potentially related to the up-regulation of Nox2 expression. Moreover, none of the repeated exposure patterns had significant effects on DNA damage, apoptosis, or autophagy, which suggested that ELF-MF exposure has no severe biological consequences in cultured hippocampal neurons.

Zhang B, Tian L. Reactive Oxygen Species: Potential Regulatory Molecules in Response to Hypomagnetic Field Exposure. Bioelectromagnetics 41(8):573-580, 2020. (Review)

Organisms, including humans, could be exposed to hypomagnetic fields (HMFs, intensity <5 μT), e.g. in some artificially shielded magnetic environments and during deep-space flights. Previous studies have demonstrated that HMF exposure could have negative effects on the

central nervous system and embryonic development in many animals. However, the underlying mechanisms remain unknown. Studies have revealed that HMFs affect cellular reactive oxygen species (ROS) levels and thereby alter physiological and biological processes in organisms. ROS, the major component of highly active free radicals, which are ubiquitous in biological systems, were hypothesized to be the candidate signaling molecules that regulate diverse physiological processes in response to changes in magnetic fields. Here, we summarize the recent advances in the study of HMF-induced negative effects on the central nervous system and early embryonic development in animals, focusing on cellular ROS and their role in response to HMFs. Furthermore, we discuss the potential mechanism through which HMFs regulate ROS levels in cells.

(NE) Zhang C, Li Y, Wang C, Lv R, Song T. Extremely low-frequency magnetic exposure appears to have no effect on pathogenesis of Alzheimer's disease in aluminum-overloaded rat. PLoS One. 8(8):e71087, 2013. (AS, CE, BE, MC, ND)

OBJECTIVE: Extremely low-frequency magnetic field (ELF-MF) has been reported to be of potential pathogenetic relevance to Alzheimer's disease (AD) for years. However, evidence confirming this function remains inconclusive. Chronic Al treatment has been identified as a contributing factor to cognitive function impairment in AD. This study aims to examine whether or not ELF-MF and Al have synergistic effects toward AD pathogenesis by investigating the effects of ELF-MF with or without chronic Al treatment on SD rats. METHODS: Sprague-Dawley (SD) rats were subjected one of the following treatments: sham (control group), oral Al (Al group), ELF-MF (100 µT at 50 Hz) with oral Al (MF+Al group), or ELF-MF (100 µT at 50 Hz) without oral Al (MF group). RESULTS: After 12 wk of treatment, oral Al treatment groups (Al and MF+Al groups) showed learning and memory impairment as well as morphological hallmarks, including neuronal cell loss and high density of amyloid-β (Aβ) in the hippocampus and cerebral cortex. ELF-MF without Al treatment showed no significant effect on AD pathogenesis. ELF-MF+Al treatment induced no more damage than Al treatment did. CONCLUSIONS: Our results showed no evidence of any association between ELF-MF exposure (100 µT at 50 Hz) and AD, and ELF-MF exposure does not influence the pathogenesis of AD induced by Al overload.

(E) Zhang H, Dai Y, Cheng Y, He Y, Manyakara Z, Duan Y, Sun G, Sun X. Influence of extremely low frequency magnetic fields on Ca^{2+} signaling and double messenger system in mice hippocampus and reversal function of procyanidins extracted from lotus seedpod. Bioelectromagnetics. 38(6):436-446, 2017. (AS, CE, CC)

This research investigated the influence of extremely low frequency magnetic fields (ELF-MF; 50 Hz, 8 mT, 4 h per day, for 28 days) on calcium ion signaling and the double messenger system in the hippocampus of mice. Messengers that were studied included: G-protein, Ins(1,4,5)P_3 (IP_3), diacylglycerol (DAG), cAMP-dependent protein kinase (PKA), and Ca^{2+} -dependent protein kinase C (PKC). The results showed that ELF-MF caused an increase in the levels of Gi protein, IP3, DAG, PKA and PKC beta, calcium and calmodulin-dependent protein phosphatase calcineuring (PP2B), and

intracellular Ca^{2+} content, and a decrease in calcium/calmodulin-dependent protein kinase II (CaMK II) and PKC alpha. In addition, ELF-MF exposure decreased the level of brain-derived neurotrophic factor (BDNF), which played a key role in hippocampal neuronal cell death. However, oral administration of procyanidins from lotus seedpod (LSPCs) (especially 90 mg kg^{-1}) significantly recovered these changes, and nearly reached normal levels. All these showed that LSPCs may mediate calcium signal and double messenger system through Ca^{2+} /CaMK II/CREB/BDNF and DG/PKC/MAPK signaling pathways to reverse the alteration caused by ELF-MF.

(E)Zhang H, Yang Y, Yang E, Tian Z, Huang Y, Zhang Z, Bao M, Liao D, Ge J, Wang C, Li X, Luo P. Pulsed Electromagnetic Fields Protect Against Brain Ischemia by Modulating the Astrocytic Cholinergic Anti-inflammatory Pathway. Cell Mol Neurobiol 43(3):1301-1317, 2023. (VT, VO, CE, AE, CC, BE, MA)

Neuroinflammation is one of the most important pathological processes following brain ischemia. Pulsed electromagnetic fields (PEMFs) protect against brain ischemia, but their role in regulating neuroinflammation remains unclear. In the present study, we investigated the biological effects of PEMF exposure on brain ischemia-induced neuroinflammation through the astrocytic cholinergic anti-inflammatory pathway. PEMF exposure reduced the activation of astrocytes and neuroinflammation following brain ischemia by directly modulating astrocytic injury and inflammatory cytokine release. Inhibition of nicotinic acetylcholine receptor alpha 7 subunit (α7nAChR) by a specific antagonist reversed the regulatory effects of PEMF on astrocytes. Furthermore, negative regulation of signal transducer and activator of transcription 3 (STAT3) by α7nAChR was found to be an important downstream mechanism through which PEMF regulates astrocyte-related neuroinflammation. PEMF suppressed STAT3 phosphorylation and nuclear translocation by activating α7nAChR. These results demonstrate that PEMF exerts anti-inflammatory effects in the context of brain ischemia by modulating astrocytic α7nAChR/STAT3 signaling.

(E) Zhang L, Geng D, Xu G, An H. [Effect of 40 Hz pulsed magnetic field on mitochondrial dynamics and heart rate variability in dementia mice]. Sheng Wu Yi Xue Gong Cheng Xue Za Zhi. 2025 Aug 25;42(4):707-715. [article in Chinese] (AS, CE, CC, EE, BE, MA, ND) (2 x 30 min/day for 14 days)

Alzheimer's disease (AD) is the most common degenerative disease of the nervous system. Studies have found that the 40 Hz pulsed magnetic field has the effect of improving cognitive ability in AD, but the mechanism of action is not clear. In this study, APP/PS1 double transgenic AD model mice were used as the research object, the water maze was used to group dementia, and 40 Hz/10 mT pulsed magnetic field stimulation was applied to AD model mice with different degrees of dementia. The behavioral indicators, mitochondrial samples of hippocampal CA1 region and electrocardiogram signals were collected from each group, and the effects of 40 Hz pulsed magnetic field on mouse behavior, mitochondrial kinetic indexes and heart rate variability (HRV) parameters were analyzed. The results showed that compared with the AD

group, the loss of mitochondrial crest structure was alleviated and the mitochondrial dynamics related indexes were significantly improved in the AD + stimulated group ($P < 0.001$), sympathetic nerve excitation and parasympathetic nerve inhibition were improved, and the spatial cognitive memory ability of mice was significantly improved ($P < 0.05$). The preliminary results of this study show that 40 Hz pulsed magnetic field stimulation can improve the mitochondrial structure and mitochondrial kinetic homeostasis imbalance of AD mice, and significantly improve the autonomic neuromodulation ability and spatial cognition ability of AD mice, which lays a foundation for further exploring the mechanism of ultra-low frequency magnetic field in delaying the course of AD disease and realizing personalized neurofeedback therapy for AD.

(E) Zhang X, Li J-F, Wu Q-J, Li B, Jiang J-C. Effects of hypomagnetic field on noradrenergic activities in the brainstem of golden hamster. Bioelectromagnetics 28(2):155-158, 2007. (AS, LE, CC, MA)

Previous studies found that elimination of the geomagnetic field (GMF) interferes with the normal brain functions, but the underlying mechanism remains unknown. The present study examined the effects of long-term exposures to a near-zero magnetic environment on the noradrenergic activities in the brainstem of golden hamsters. Both the content of norepinephrine (NE) and the density of NE-immunopositive neurons in the tissue decreased significantly after the treatment, and the effects could be progressive with time. These variations may substantially contribute to behavioral and mood disorders reported in other studies when animals are shielded from the GMF.

(E) Zhang X, Lv M, Zhu X, Tian L, Li J, Shao Y, Gao C, Sun X. Isoflurane preconditioning ameliorates electromagnetic pulse-induced neural damage by shifting microglia polarization toward anti-inflammatory phenotype via upregulation of SOCS1. Int Immunopharmacol. 68:48-57, 2019. (AS, CE, FC, MA)

With the speedy technological advances during the past few decades, human exposure to the electromagnetic field (EMF) has become increasingly common. Exposure to EMF may induce neural injuries and dysfunction of various organs, likely involving neuroinflammation and activation of microglial cells. Isoflurane preconditioning (IP) is shown to provide neuroprotection in various neurological diseases by inhibiting excessive neuroinflammatory responses. Brain samples harvested from rats exposed to electromagnetic pulse (EMP) with or without IP were subjected to qPCR, Western blot assay, and immunohistochemistry to determine the expression of pro-inflammatory/anti-inflammatory microglia markers and a variety of pro- and anti-inflammatory mediators. Suppressor of cytokine signaling 1 (SOCS1) siRNA was used in cultured N9 microglia cells to examine the roles of SOCS1 in the effect of IP. In both in vivo and in vitro experiments, EMP-exposed microglia were predominantly pro-inflammatory microglia, accompanied by increased expression of pro-inflammatory cytokines and chemokines, and activation of TLR4 pathway, leading to neuronal death. IP reversed the changes induced by EMP and switched the activated microglia to an anti-inflammatory phenotype. SOCS1 siRNA abolished the beneficial effects of IP. IP ameliorates EMP-

induced neural injuries by shifting microglia polarization from pro-inflammatory to anti-inflammatory phenotype via upregulation of SOCS1.

(E) Zhang X-J, Xiao Z-B, Gu J-X, Chen K, Wang J, Xu S-L, Xing K-K, Chen T. Investigating the molecular mechanisms of delirium-like neuropsychiatric disorder induced by electromagnetic pulse based on bioinformatics analysis. Mol Brain 16(1):21, 2023. (AS, CE, BE, CC)

Electromagnetic pulse (EMP), a unique type of electromagnetic radiation, may induce diverse neuropsychiatric disorders, such as irritability, hyperkinesis, retardation of learning and memory. However, the underlying mechanism of EMP exposure on neuronal injury has not been elucidated. Here, we aimed to delineate the regulatory expression networks based on high-throughput sequencing data to explore the possible molecular mechanisms related to EMP-induced delirium-like neuropsychiatric disorder in rats. It's shown that EMP exposure induced anxiety, cognitive decline and short-term memory impairment. The expression profiles of the long noncoding RNAs (lncRNAs) and mRNAs, along with their biological function and regulatory network, were explored in rats after EMP exposure. We identified 41 differentially expressed lncRNAs (DELs) and 266 differentially expressed mRNAs (DEMs) between EMP and sham groups. Sixty-one co-expression relationships between 18 DELs and 56 DEMs were mostly associated with synapse- and metabolic-related pathways. We predicted 51 DEL-miRNA pairs and 290 miRNA-mRNA pairs using the miRanda database to constructed a DEL-miRNA-DEM network. LncRNA AABR07042999.1 and mRNA Tph2, Slc6a4, Dbh and Th were upregulated, and the contents of serotonin, dopamine and norepinephrine were increased in both PFC and HIP after EMP exposure. The current study provided a better understanding of the ceRNA network, which might reveal the pathological mechanism and provide more treatment options for the EMP-induced neurobehavioral disorder.

(E) Zhang X-Q, Li L, Huo J-T, Cheng M, Li L-H. Effects of repetitive transcranial magnetic stimulation on cognitive function and cholinergic activity in the rat hippocampus after vascular dementia. Neural Regen Res 13(8):1384-1389, 2018. (AS, CE, BE, MC, CC, MA)

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive treatment that can enhance the recovery of neurological function after stroke. Whether it can similarly promote the recovery of cognitive function after vascular dementia remains unknown. In this study, a rat model for vascular dementia was established by the two-vessel occlusion method. Two days after injury, 30 pulses of rTMS were administered to each cerebral hemisphere at a frequency of 0.5 Hz and a magnetic field intensity of 1.33 T. The Morris water maze test was used to evaluate learning and memory function. The Karnovsky-Roots method was performed to determine the density of cholinergic neurons in the hippocampal CA1 region. Immunohistochemical staining was used to determine the number of brain-derived neurotrophic factor (BDNF)-immunoreactive cells in the hippocampal CA1 region. rTMS treatment for 30 days significantly improved learning and memory function, increased acetylcholinesterase and choline acetyltransferase activity, increased the density of cholinergic neurons, and increased the number of BDNF-immunoreactive cells. These results indicate that rTMS can ameliorate learning and memory deficiencies in rats with vascular dementia. The mechanism through which this occurs might be related to the promotion

of BDNF expression and subsequent restoration of cholinergic system activity in hippocampal CA1 region.

(NE) Zhang Y, Liu X, Zhang J, Li N. Short term effects of extremely low frequency electromagnetic fields exposure on Alzheimer's disease in rats. Int J Radiat Biol. 91(1):28-34, 2015. (AS, CE, BE, ND)

Purpose: With the development and widespread use of electromagnetic field (EMF) technology, recent studies are focusing on the effects of EMF on human health. Recently, extremely low frequency electromagnetic fields (ELF-EMF) have been studied with great interest due to their possible effects on Alzheimer's disease (AD). The objective of the present study was to investigate the interaction between ELF-EMF exposure and memory impairment in rats. Materials and methods: Twenty healthy male Sprague Dawley (SD) rats were randomly divided into two groups (n=10). Animals were exposed to 100µT/50Hz ELF-EMF or subjected to sham exposure when 12 weeks old. After 12 weeks, Morris water maze (MWM) was used to test the changes in cognitive and memory ability. Amyloid-beta (Aβ) content in cortex, hippocampus and plasma were measured by ELISA assays. The morphology of neuron was detected by HE staining. Results: After exposure, the body weight of rats showed no difference compared with control group. The application of ELF-EMF did not induce any cognitive and memory impairment compared with sham exposure group. The determination of Aβ showed no significant change between two groups. And there was no histological change in ELF-EMF exposure group. Conclusion: The present study indicated that short term exposure of 100µT/50Hz ELF-EMF had no effects on cognition and memory of rats, and did not alter the expression of Aβ and the neuron morphology. However, more comprehensive studies are still required to elucidate the possible effects and underlying mechanisms of ELF-EMF exposure on living organisms.

(NE) Zhang Y, Liu X, Zhang J, Li N. Short-term effects of extremely low frequency electromagnetic fields exposure on Alzheimer's disease in rats. Int J Radiat Biol. 91(1):28-34, 2015. (AS, CE, BE, MA, ND, CC)

PURPOSE: With the development and widespread use of electromagnetic field (EMF) technology, recent studies are focusing on the effects of EMF on human health. Recently, extremely low frequency electromagnetic fields (ELF-EMF) have been studied with great interest due to their possible effects on Alzheimer's disease (AD). The objective of the present study was to investigate the interaction between ELF-EMF exposure and memory impairment in rats. **MATERIALS AND METHODS:** Twenty healthy male Sprague Dawley (SD) rats were randomly divided into two groups (n = 10). Animals were exposed to 100 µT/50 Hz ELF-EMF or subjected to sham exposure when 12 weeks old. After 12 weeks, the Morris water maze (MWM) was used to test the changes in cognitive and memory ability. Amyloid-beta (Aβ) content in cortex, hippocampus and plasma were measured by ELISA assays. The morphology of neuron was detected by H&E staining. **RESULTS:** After exposure, the body weight of rats showed no difference compared with the control group. The application of ELF-EMF did

not induce any cognitive and memory impairment compared with the sham-exposure group. The determination of Aβ showed no significant change between the two groups, and there was no histological change in ELF-EMF exposure group. **CONCLUSION:** The present study indicated that short-term exposure of 100 μT/50 Hz ELF-EMF had no effects on cognition and memory of rats, and did not alter the expression of Aβ and the neuron morphology. However, more comprehensive studies are still required to elucidate the possible effects and underlying mechanisms of ELF-EMF exposure on living organisms.

(E) Zhao QR, Lu JM, Yao JJ, Zhang ZY, Ling C, Mei YA. Neuritin reverses deficits in murine novel object associative recognition memory caused by exposure to extremely low-frequency (50 Hz) electromagnetic fields. Sci Rep. 5:11768, 2015. (AS, CE, BE, MA)

Animal studies have shown that electromagnetic field exposure may interfere with the activity of brain cells, thereby generating behavioral and cognitive disturbances. However, the underlying mechanisms and possible preventions are still unknown. In this study, we used a mouse model to examine the effects of exposure to extremely low-frequency (50 Hz) electromagnetic fields (ELF MFs) on a recognition memory task and morphological changes of hippocampal neurons. The data showed that ELF MFs exposure (1 mT, 12 h/day) induced a time-dependent deficit in novel object associative recognition memory and also decreased hippocampal dendritic spine density. This effect was observed without corresponding changes in spontaneous locomotor activity and was transient, which has only been seen after exposing mice to ELF MFs for 7-10 days. The over-expression of hippocampal neuritin, an activity-dependent neurotrophic factor, using an adeno-associated virus (AAV) vector significantly increased the neuritin level and dendritic spine density. This increase was paralleled with ELF MFs exposure-induced deficits in recognition memory and reductions of dendritic spine density. Collectively, our study provides evidence for the association between ELF MFs exposure, impairment of recognition memory, and resulting changes in hippocampal dendritic spine density. Neuritin prevented this ELF MFs-exposure-induced effect by increasing the hippocampal spine density.

(E) Zhao W, Dong L, Tian L, Zhao L, Zhao Y, Zheng Y. Changes in intracellular calcium concentration level accompany age-related inhibitions of Long-term potentiation in hippocampus induced by Extremely low frequency electromagnetic fields. Eur J Neurosci 58(2):2437-2450, 2023. (CS, AE, EE, DE)

Extremely low frequency electromagnetic fields (ELF-EMFs) have received increasing attention and in-depth research due to their ability to affect learning and memory functions. However, its regulation and intrinsic mechanism at different ages in early developmental stages remains unclear. In this article, the regulation of 15 Hz/2 mT ELF-EMFs on Long-term potentiation (LTP) persistence in the hippocampal CA1 region of Sprague-Dawley (SD) rats at early developmental stages (8, 15, 22, and 29-day-old) are investigated by electrophysiological techniques. The results shows that ELF-EMFs differentially inhibit LTP persistence due to age difference, and the younger age, the more significant the inhibitory effect. Secondly, the inhibitory effect of ELF-EMFs on LTP persistence disappeared after the addition of 2-

Aminoethoxydiphenyl borate (2-APB) to block inositol-1,4,5-trisphosphate receptors (IP3 Rs) localized to intracellular calcium stores to reduce the intracellular calcium concentration ([Ca2+]i), proving that the LTP persistence regulated by ELF-EMFs is associated with the IP3 Rs-mediated intracellular calcium stores. Finally, the level of [Ca2+]i was intervened by adjusting the extracellular calcium concentration([Ca2+]e). Interestingly, the inhibitory effect of ELF-EMFs on LTP persistence in the 15-day-old group disappeared by increasing [Ca2+]e , while the inhibitory effect of ELF-EMFs on LTP persistence in the 29-day-old group appeared by decreasing [Ca2+]e . Our findings reveal the underlying mechanism of the effect of ELF-EMFs on synaptic plasticity in hippocampal CA1 area at early developmental stages, and provide new insights into more rational application and protection of ELF-EMFs.

(E) Zhen J, Qian Y, Fu J, Su R, An H, Wang W , Zheng Y, Wang X. Deep Brain Magnetic Stimulation Promotes Neurogenesis and Restores Cholinergic Activity in a Transgenic Mouse Model of Alzheimer's Disease. Front Neural Circuits. 11:48, 2017. (AS, CE, MC, ND, MA)

Alzheimer's disease (AD) is characterized by progressive decline of memory and cognitive functions. Deep magnetic stimulation (DMS), a noninvasive and nonpharmacological brain stimulation, has been reported to alleviate stress-related cognitive impairment in neuropsychiatric disorders. Our previous study also discovered the preventive effect of DMS on cognitive decline in an AD mouse model. However, the underlying mechanism must be explored further. In this study, we investigated the effect of DMS on spatial learning and memory functions, neurogenesis in the dentate gyrus (DG), as well as expression and activity of the cholinergic system in a transgenic mouse model of AD (5XFAD). Administration of DMS effectively improved performance in spatial learning and memory of 5XFAD mice. Furthermore, neurogenesis in the hippocampal DG of DMS-treated 5XFAD mice was clearly enhanced. In addition, DMS significantly raised the level of acetylcholine and prevented the increase in acetylcholinesterase activity as well as the decrease in acetyltransferase activity in the hippocampus of 5XFAD mice. These findings indicate that DMS may be a promising noninvasive tool for treatment and prevention of AD cognitive impairment by promoting neurogenesis and enhancing cholinergic system function.

(E) Zheng Y, Ma W, Dong L, Dou JR, Gao Y, Xue J. Influence of the on-line ELF-EMF stimulation on the electrophysiological properties of the rat hippocampal CA1 neurons in vitro. Rev Sci Instrum. 88(10):105106, 2017. (CS, AE, CC, EE)

The extremely low frequency electromagnetic fields (ELF-EMFs) have been shown to have an environmentally negative effect on humans' health; however, its treatment effect is beneficial for patients suffering from neurological disorders. Despite this success, the application of ELF-EMF has exceeded in the understanding of its internal mechanism. Recently, it was found that on-line magnetic stimulation may offer advantages over off-line magnetic exposure and has proven to be effective in activating the prefrontal cortex pyramidal neurons in vitro. Here, we perform computational simulations of the stimulation coils in COMSOL modeling to describe the uniformity of

the distribution of the on-line magnetic field. Interestingly, the modeling data and actual measurements showed that the densities of the magnetic flux that was generated by the on-line stimulation coils were similar. The on-line magnetic stimulator induced sodium channel currents as well as field excitatory postsynaptic potentials of the rat hippocampal CA1 neurons and successfully demonstrated its extensive applications to activate neuronal tissue. These findings further raise the possibility that the instrument of on-line magnetic stimulation may be an effective alternative for studies in the field of bioelectromagnetics.

(E) Zheng Y, Dou JR, Gao Y, Dong L, Li G. Effects of 15 Hz square wave magnetic fields on the voltage-gated sodium and potassium channels in prefrontal cortex pyramidal neurons. Int J Radiat Biol. 93(4):449-455, 2017. (CS, AE, FC)

PURPOSE: Although magnetic fields have significant effects on neurons, little is known about the mechanisms behind their effects. The present study aimed to measure the effects of magnetic fields on ion channels in cortical pyramidal neurons. MATERIALS AND METHODS: Cortical pyramidal neurons of Kunming mice were isolated and then subjected to 15 Hz, 1 mT square wave (duty ratio 50%) magnetic fields stimulation. Sodium currents (I_{Na}), transient potassium currents (I_A) and delayed rectifier potassium currents (I_K) were recorded by whole-cell patch clamp method. RESULTS: We found that magnetic field exposure depressed channel current densities, and altered the activation kinetics of sodium and potassium channels. The inactivation properties of I_{Na} and I_A were also altered. CONCLUSION: Magnetic field exposure alters ion channel function in neurons. It is likely that the structures of sodium and potassium channels were influenced by the applied field. Sialic acid, which is an important component of the channels, could be the molecule responsible for the reported results.

(E) Zheng Y, Ma XX, Dong L, Gao Y, Tian L. Effects of single- and hybrid-frequency extremely low-frequency electromagnetic field stimulations on long-term potentiation in the hippocampal Schaffer collateral pathway. Int J Radiat Biol. 95(9):1319-1325, 2019. (CS, AE, EE)

Purpose: To study the different effects of single- and hybrid-frequency magnetic fields on long-term potentiation (LTP) in synaptic plasticity. **Materials and methods:** Based on the online electromagnetic field stimulation system and field excitatory postsynaptic potentials (fEPSPs) recording system, we applied four different single- and hybrid-frequency magnetic fields with an intensity of 1 mT to the Schaffer collateral (CA1) pathway of rat hippocampal slices in vitro. **Results:** The amplitude of fEPSPs decreased significantly under both single- and hybrid-frequency magnetic stimulation. Lower single-frequency magnetic stimulation on LTP had a greater regulating effect, while the regulating effect among four different hybrid-frequency extremely low-frequency electromagnetic fields (ELF-EMFs) stimulations on LTP showed no significant differences. **Conclusion:** Single-frequency magnetic stimulation produces more significant regulatory effects, and the lower the frequency, the more significant the regulatory effect. The effect of hybrid-frequency magnetic stimulation in each group was similar, and there was no significant difference between each group. The 15-Hz single-frequency magnetic stimulation group showed the most significant regulatory effect, but once it was mixed with other higher frequency magnetic stimulation, its regulation effect was significantly weakened.

(E) Zheng Y, Cheng J, Dong L, Ma X, Kong Q. Effects of exposure to extremely low frequency electromagnetic fields on hippocampal long-term potentiation in hippocampal CA1 region. Biochem Biophys Res Commun. 517(3):513-519,.2019 (CS, AE, EE)

Exposure to environmental electromagnetic fields, especially to the extremely low-frequency (ELF < 300 Hz) electromagnetic fields (EMFs) might produce modulation effects on neuronal activity. Long-term changes in synaptic plasticity such as long-term potentiation (LTP) involved in learning and memory may have contributions to a number of neurological diseases. However, the modulation effects of ELF-EMFs on LTP are not yet fully understood. In our present study, we aimed to evaluate the effects of exposure to ELF-EMFs on LTP in hippocampal CA1 region in rats. Hippocampal slices were exposed to magnetic fields generated by sXcELF system with different frequencies (15, 50, and 100 Hz [Hz]), intensities (0.5, 1, and 2 mT [mT]), and duration (10 s [s], 20 s, 40 s, 60 s, and 5 min), then the baseline signal recordings for 20 min and the evoked field excitatory postsynaptic potentials (fEPSPs) were recorded. We found that the LTP amplitudes decreased after magnetic field exposure, and the LTP amplitudes decreased in proportion to exposure doses and durations, suggesting ELF-EMFs may have dose and duration-dependent inhibition effects. Among multiple exposure duration and doses combinations, upon 5 min magnetic field exposure, 15 Hz/2 mT maximally inhibited LTP. Under 15 Hz/2 mT ELF-EMFs, LTP amplitude decreases in proportion to the length of exposure durations within 5 min time frame. Our findings illustrated the potential effects of ELF-EMFs on synaptic plasticity and will lead to better understanding of the influence on learning and memory.

(E) Zheng Y, Ma XX, Dong L, Ma W, Cheng JH. Effects of uninterrupted sinusoidal LF-EMF stimulation on LTP induced by different combinations of TBS/HFS at the Schaffer collateral-CA1 of synapses. Brain Res. 1725:146487, 2019. (CS, AE, EE, CC)

Long-term potentiation (LTP) is an important aspect of synaptic plasticity and is one of the main mechanisms involved in memory. Low-frequency electromagnetic fields (LF-EMFs) such as transcranial magnetic stimulation are emerging neuromodulation tools for the regulation of LTP. However, whether LF-EMFs have different effects on different types of LTP has not yet been verified. Herein, we studied the regulatory effects of 15 Hz/2 mT sinusoidal magnetic field as pre-magnetic stimulation on several types of LTP, which were induced by theta-burst(TBS) or high-frequency stimulation (HFS) or some combination of them, and applied N-methyl-D-aspartate receptor(NMDAR) antagonists to observe the relationship between the regulation of LTP by LF-EMFs and NMDAR in the Schaffer collateral pathway of rat brain slices in vitro. The results presented in this paper are the performance of TBS and HFS was not exactly the same and the recovery speed of TBS-LTP was faster than HFS-LTP after receiving the regulation of LF-EMFs; moreover, the LTP level was affected by the order of combination and the effect of pre-magnetic stimulation could maintain the entire process of the combined induction experiment, while NMDAR antagonists could not completely offset the influence of LF-EMFs. The memory patterns are diverse, and this study has shown LF-EMFs can regulate LTP such as TBS-LTP and HFS-LTP and can continuously affect multiple LTP induction processes. However, different memory processes may have different performance in the face of

LF-EMFs regulation. In terms of the mechanism of LF-EMFs-induced LTP regulation, NMDARs may be involved in the process of LF-EMF regulation of LTP, but are not the only factor.

Zheng Y, Xia P, Dong L, Tian L, Xiong C. Effects of modulation on sodium and potassium channel currents by extremely low frequency electromagnetic fields stimulation on hippocampal CA1 pyramidal cells. Electromag. Biol. Med. 40(2):274-285, 2021.

To investigate the effects of extremely low-frequency electromagnetic fields (ELF-EMFs) stimulation on sodium channel currents (I_{Na}), transient outward potassium channel currents (I_A) and delayed rectifier potassium channel currents (I_K) on hippocampal CA1 pyramidal neurons of young Sprague Dawley rats. CA1 pyramidal neurons of rat hippocampal slices were subjected to ELF-EMFs stimulation with different frequencies (15 and 50 Hz), intensities (0.5, 1 and 2 mT) and durations (10, 20 and 30 min). The I_{Na}, I_A and I_K of neurons were recorded by a whole-cell patch-clamp method. ELF-EMFs stimulation enhanced I_{Na} densities, and depressed I_A and I_K densities. In detail, I_{Na} was more sensitive to the variation of intensities and frequencies of ELF-EMFs, whereas I_A and I_K were mainly affected by the variation of the duration of ELF-EMFs. ELFEMFs stimulation altered activation and deactivation properties of I_{Na}, I_A and I_K. ELF EMFs stimulation plays a role as a regulator rather than an inducer for ion channels. It might change the transition probability of ion channel opening or closing, and might also change the structure and function of the ion channel which need to be proved by the further technical method.

(E) Zheng Y, Zhao W, Ma X, Dong L, Tian L, Zhou M Comparison of ELF-EMFs stimulation with current stimulation on the regulation of LTP of SC-CA1 synapses in young rat hippocampus. Int J Radiat Biol 97(7):1032-1041, 2021. (CS, AE, EE, FC)

Background: Long-term potentiation (LTP) is an important functional indicator for synaptic plasticity. Extremely low frequency electromagnetic fields (ELF-EMFs) are a physical means to regulate LTP, which induce induced currents. It is unknown whether induced current is the key factor when LTP is regulated by ELF-EMFs. New Method: A method is proposed for calculating the current value induced by ELF-EMFs. Then, a comparison of ELF-EMFs with current on the regulation of theta-burst or high-frequency stimulation (TBS/HFS)-LTP was performed. **Results:** The LTP after ELF-EMFs and μA current regulation was significantly reduced. The regulatory effect of 0.1 μA current on LTP was similar with 100 Hz/2 mT ELF-EMFs, while 0.2 μA had a stronger regulatory effect than 200 Hz/2 mT on HFS-LTP. Comparison with Existing Methods: Most of the existing methods were used to calculate the induced current in human models, while we present a more accurate model for calculating the induced current induced by ELF-EMFs in the rat brain slices. **Conclusions:** This work indicated that μA current and ELF-EMFs stimulation reduced LTP. Also, we demonstrated that the regulatory effect of ELF-EMFs on LTP is not entirely deriving from the induced current, since its magnetic mechanism might have played a certain role.

(E) Zheng Y, Zhao L, Dong L, Tian C, Xia P, Jin Z. The Time-Dependence of Three Different Modes of ELF-EMF Stimulation on LTP at Schaffer Collateral-CA1 Synapses. Bioelectromagnetics 42(7):538-549, 2021. (CS, AE, EE)

Long-term potentiation (LTP) is considered the cellular basis of learning and memory. Extremely low-frequency electromagnetic fields (ELF-EMFs) are neuromodulation tools for regulating LTP. However, the temporal effects of short-term ELF-EMF stimulation on LTP are not yet known. In this study, we evaluated the time-dependent effects of 15 Hz/2 mT ELF-EMF stimulation on LTP at the Schaffer collateral-CA1 (SC-CA1) synapses in Sprague-Dawley rats. Hippocampal slices were exposed to three different modes of ELF-EMFs (sinusoidal, single-frequency pulse, and rhythm pulse) and durations (10, 20, 40, and 60 s). The baseline was recorded for 20 min and field excitatory postsynaptic potential (fEPSP) was recorded for 60 min using multi-electrode arrays (MEA) after plasticity induction using 100 Hz electrical high-frequency stimulation (HFS). Compared to the control group, the LTP decreased under three different magnetic fields and was proportional to time; that is, the longer the time, the greater the inhibition. We also compared the three magnetic fields and showed that the continuous sinusoidal magnetic field had the largest inhibitory rate of LTP, while pulsed and rhythm pulsed magnetic fields were similar. We showed that different modes of ELF-EMF stimulation had a time-dependent effect on LTP at Schaffer collateral-CA1 synapses, which provides experimental evidence for the treatment of related neurological diseases.

(E) Zheng Y, Wang M, Dong L, Tian C, Qi D, Chen Y. Effect of three different frequencies of micro-magnetic stimulation on the neuronal electrical activity of the hippocampal CA1 neurons in mice. Neuroscience 2025 Mar 1:S0306-4522(25)00181-2. doi: 10.1016/j.neuroscience.2025.02.057. Online ahead of print. (CS, AE, EE)

Frequency is essential in regulating neuroelectric activity using magnetic fields. Current reports focus on 100 Hz or less. Studying other relatively high magnetic stimulation frequencies is necessary to reveal the influence of magnetic stimulation frequency parameters on electrical activity. This paper examined the pyramidal neurons in the CA1 region of the hippocampus of C57 mice. A custom-built micro-magnetic stimulation (μMS) device with sub-millimeter dimensions was utilized. Three magnetic field frequencies of 15 Hz, 3 kHz, and 70 kHz were chosen at a magnetic field strength of 1 mT. Precision-targeted magnetic stimulation of CA3 area neurons upstream of CA1 by whole-cell membrane clamp method. The effects of three various magnetic stimulation frequencies on the action potential (AP), sodium channel current (INa), and transient outward potassium channel current (IA) of neurons in the hippocampal CA1 area were investigated. 15 Hz inhibited the excitability of pyramidal neurons within the CA1 area; 3 kHz had a facilitating effect, while the 70 kHz magnetic stimulation had a more pronounced facilitating effect. Magnetic field stimulation at 15 Hz decreased neuronal excitability, whereas magnetic field stimulation at 3 and 70 kHz increased neuronal excitability.

(E) Ziegenbalg L, Güntürkün O, Winklhofer M. Extremely low frequency magnetic field distracts zebrafish from a visual cognitive task. Sci Rep. 15(1):8589, 2025. (AS, CE, BE)

Electromagnetic fields emitted from overhead power lines and subsea cables are widely regarded to be a disruptive factor for animals using the natural magnetic field as orientation cue for

guiding their directed movements. However, it is not known if anthropogenic electromagnetic fields also have the potential to disturb animals attending to information from other sensory modalities. To find out, we trained adult zebrafish (*Danio rerio*) individually to perform avoidance behavior in response to a visual signal (green LED light spot), which in the exposure group was presented simultaneously with a sinusoidally changing magnetic field (0.3 Hz, group A: 0.015 mT, group B: 0.06 mT). Despite the salience of the visual signal, which was both sufficient and necessary to elicit conditioned avoidance responses, the 0.06 mT magnetic condition had a negative impact on learning performance and response behavior. This suggests that extremely low frequency technical magnetic fields of Earth strength amplitude can act as cross-modal distractor that diverts the attention of animals away from environmentally relevant cues based on nonmagnetic sensory modalities. Our research highlights the need to study the role of anthropogenic magnetic fields as sensory pollutant beyond the scope of magnetic orientation behavior.

Zou D-F, Li Z-H, Liu Y-B, Wang C-Z. Progress in the study of the effects of electromagnetic radiation on the mood and rhythm. Electromagn Biol Med 2025 Feb 18:1-16. doi: 10.1080/15368378.2025.2460971. Online ahead of print. (Review)

The ever-expanding use of a large number of electrical appliances and mobile communication systems, which outnumber the global population, emit electromagnetic radiation through mobile telephones, power stations, transmission lines, radar, microwave ovens, televisions, refrigerators, therapeutic and other electronic devices. Electromagnetic radiation has been classified by the International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans (Group 2B). A large number of research results show that short-term and long-term exposure to electromagnetic radiation can lead to anxiety, depression, decreased learning ability, memory loss, sleep rhythm disorders and other adverse effects. Sleep rhythm disorders affect many people worldwide and may be associated with psychiatric disorders such as anxiety and depression. In this review, we summarise key experiments related to the effects of electric field exposure on mood and rhythms in animal and cellular studies over the past decade, describe the effects of electromagnetic radiation on emotional behaviors and circadian rhythms in humans and mammals, and explore the relationship between electromagnetic radiation, mood and rhythms as well as its underlying mechanisms of action. Most animal studies suggest that electromagnetic radiation may affect the physiological organization and functioning of the brain, influence neurotransmitters and receptors, interfere with neuronal formation and structure, or alter associated endocrine hormones and free radicals, which may lead to the unfavorable development of psychiatric disorders and sleep rhythm disorders. This summary may provide researchers with better clues and ideas to develop therapeutic solutions with sleep disorders and depressive psychiatric disorders.

(E) Zuo H, Liu X, Wang D, Li Y, Xu X, Peng R, Song T. RKIP-Mediated NF-κB Signaling is involved in ELF-MF-mediated improvement in AD rat. Int J Med Sci. 15(14):1658-1666, 2018. (AS, CE, CC, BE, MA, ND)

In a previous study, we reported the positive effects of extremely low frequency electromagnetic field (ELF-MF) exposure on Alzheimer's disease (AD) rats; however, the underlying mechanism remains unclear. In addition, we found that Raf-1 kinase inhibitor protein (RKIP) was downregulated by microwave exposure in the rat

hippocampus. Our hypothesis was that RKIP-mediated NF-κB pathway signaling is involved in the effect of ELF-MF on the AD rat. In this study, D-galactose intraperitoneal (50 mg/kg/d for 42 d) and $A\beta_{25-35}$ hippocampal (5 μL/unilateral, bilateral, single-dose) injection were implemented to establish an AD rat model. Animals were exposed to 50 Hz and 400 μT ELF-MF for 60 continuous days. The spatial memory ability of the rat was then tested using the Morris water maze. Protein expression and interaction were detected by western blotting and co-immunoprecipitation for RKIP-mediated NF-κB pathway factors. The results showed that ELF-MF exposure partially improved the cognitive disorder, upregulated the levels of RKIP, TAK1, and the RKIP/TAK1 interaction, but downregulated p-IKK levels in AD rats. These results indicated that RKIP-mediated NF-κB pathway signaling plays an important role in the ELF-MF exposure-mediated improvements in the AD rat. Our study suggested that ELF-MF exposure might have a potential therapeutic value for AD. Further in depth studies are required in the future.