December 14, 2017

Literature on neurological effects of radiofrequency radiation (2007-2017)

Below is a key to abbreviations used throughout the following list of abstracts for papers published since 2007 and serve as my comments to help the readers identify the significance of each paper.

(E)-effect observed; (NE)- no significant effect observed; HU- human study; AS- animal study; CS-cell study; LI- low intensity/cell tower; CE- chronic/repeated exposure; BE- behavioral effect; DE- developmental effect; CC- cellular effects; CH-chemical changes; ME-morphological effect; PE-physiological effect; EE- electrophysiological effect; OX- oxidative changes; AD- age-dependent effect; SL- effect on sleep; MA- possible medical application; WS- waveform specific effect; IA- interaction with other factors.

Total number of papers=325; E=235 (72%); NE=90 (28%)

(E) Abdel-Rassoul G, El-Fateh OA, Salem MA, Michael A, Farahat F, El-Batanouny M, Salem E. Neurobehavioral effects among inhabitants around mobile phone base stations. Neurotoxicology. 28(2):434-440, 2007. (HU, CE, BE, LI, SL)

BACKGROUND: There is a general concern on the possible hazardous health effects of exposure to radiofrequency electromagnetic radiations (RFR) emitted from mobile phone base station antennas on the human nervous system. AIM: To identify the possible neurobehavioral deficits among inhabitants living nearby mobile phone base stations. METHODS: A cross-sectional study was conducted on (85) inhabitants living nearby the first mobile phone station antenna in Menoufiya governorate, Egypt, 37 are living in a building under the station antenna while 48 opposite the station. A control group (80) participants were matched with the exposed for age, sex, occupation and educational level. All participants completed a structured questionnaire containing: personal, educational and medical histories; general and neurological examinations; neurobehavioral test battery (NBTB) [involving tests for visuomotor speed, problem solving, attention and memory]; in addition to Eysenck personality questionnaire (EPQ). RESULTS: The prevalence of neuropsychiatric complaints as headache (23.5%), memory changes (28.2%), dizziness (18.8%), tremors (9.4%), depressive symptoms (21.7%), and sleep disturbance (23.5%) were significantly higher among exposed inhabitants than controls: (10%), (5%), (5%), (0%), (8.8%) and (10%), respectively ($P<0.05$). The NBTB indicated that the exposed inhabitants exhibited a significantly lower performance than controls in one of the tests of attention and short-term auditory memory [Paced Auditory Serial Addition Test (PASAT)]. Also, the inhabitants opposite the station exhibited a lower performance in the problem solving test (block design) than those under the station. All inhabitants exhibited a better performance in the two tests of visuomotor speed (Digit symbol and Trailmaking B) and one test of attention (Trailmaking A) than controls. The last available measures of RFR emitted from the first mobile phone base station antennas in Menoufiya governorate were less than the allowable standard level. CONCLUSIONS AND RECOMMENDATIONS: Inhabitants living nearby mobile phone base

stations are at risk for developing neuropsychiatric problems and some changes in the performance of neurobehavioral functions either by facilitation or inhibition. So, revision of standard guidelines for public exposure to RER from mobile phone base station antennas and using of NBTB for regular assessment and early detection of biological effects among inhabitants around the stations are recommended.

(E) Aboul Ezz HS, Khadrawy YA, Ahmed NA, Radwan NM, El Bakry MM. The effect of pulsed electromagnetic radiation from mobile phone **on the levels of monoamine neurotransmitters in four different areas of rat brain. Eur Rev Med Pharmacol Sci. 17(13):1782-1788, 2013. (AS, CE, CH)**

BACKGROUND: The use of **mobile** phones is rapidly increasing all over the world. Few studies deal with the effect of electromagnetic radiation (EMR) on monoamine neurotransmitters in the different brain areas of adult rat. AIM: The aim of the present study was to investigate the effect of EMR on the concentrations of dopamine (DA), norepinephrine (NE) and serotonin (5-HT) in the hippocampus, hypothalamus, midbrain and medulla oblongata of adult rats. MATERIALS AND METHODS: Adult rats were exposed daily to EMR (frequency 1800 MHz, specific absorption rate 0.843 W/kg, power density 0.02 mW/cm2, modulated at 217 Hz) and sacrificed after 1, 2 and 4 months of daily EMR exposure as well as after stopping EMR for 1 month (after 4 months of daily EMR exposure). Monoamines were determined by high performance liquid chromatography coupled with fluorescence detection (HPLC-FD) using their native properties. RESULTS: The exposure to EMR resulted in significant changes in DA, NE and 5-HT in the four selected areas of adult rat brain. CONCLUSIONS: The exposure of adult rats to EMR may cause disturbances in monoamine neurotransmitters and this may underlie many of the adverse effects reported after EMR including memory, learning, and stress.

***(E) Abramson MJ, Benke GP, Dimitriadis C, Inyang IO, Sim MR, Wolfe RS, Croft RJ. Mobile telephone use is associated with changes in cognitive function in young adolescents. Bioelectromagnetics. 30(8):678-686, 2009. (HU, BE) (*Effects observed probably not caused by exposure to RFR.)**

As part of the Mobile Radiofrequency Phone Exposed Users' Study (MoRPhEUS), a cross-sectional epidemiological study examined cognitive function in secondary school students. We recruited 317, 7th grade students (144 boys, 173 girls, median age 13 years) from 20 schools around Melbourne, Australia. Participants completed an exposure questionnaire based on the Interphone study, a computerised cognitive test battery, and the Stroop colour-word test. The principal exposure metric was the total number of reported mobile phone voice calls per week. Linear regression models were fitted to cognitive test response times and accuracies. Age, gender, ethnicity, socio-economic status and handedness were fitted as covariates and standard errors were adjusted for clustering by school. The accuracy of working memory was poorer, reaction time for a simple learning task shorter, associative learning response time shorter and accuracy poorer in children reporting more mobile phone voice calls. There were no significant relationships between exposure and signal detection, movement monitoring or

estimation. The completion time for Stroop word naming tasks was longer for those reporting more mobile phone voice calls. The findings were similar for total short message service (SMS, also known as text) messages per week, suggesting these cognitive changes were unlikely due to radiofrequency (RF) exposure. Overall, mobile phone use was associated with faster and less accurate responding to higher level cognitive tasks. These behaviours may have been learned through frequent use of a mobile phone.

(NE) Ahlers MT, Ammermüller J. No influence of acute RF exposure (GSM-900, GSM-1800, and UMTS) on mouse retinal ganglion cell responses under constant temperature conditions. Bioelectromagnetics. 2013 Sep 21. doi: 10.1002/bem.21811. [Epub ahead of print] (CS, CC)

Possible non-thermal effects of radio frequency electromagnetic fields (RF-EMF) on retinal ganglion cells were studied in vitro under conditions of constant temperature. Isolated mouse retinae were exposed to GSM-900, GSM-1800, and universal mobile telecommunication system (UMTS) RF-EMF applying specific absorption rates (SAR) of 0 (sham), 0.02, 0.2, 2, and 20 W/kg. Temperature was kept constant within ±0.5 to 1 °C for GSM-900 and ±0.5 °C for GSM-1800 and UMTS. Responses of retinal ganglion cells to light stimuli of three intensities (0.5, 16, and 445 lx) were recorded before, during, and up to 35 min after exposure. Experiments were performed under double-blind conditions. Changes in light responses during and after exposure were determined for each condition (RF-EMF; SAR value; light intensity) with respect to the responses before exposure, respectively. Changes were calculated using the Euclidian distance of the n-dimensional response vectors, respectively. Some changes already occurred during sham (0 W/kg) exposure, reflecting the intrinsic variability in retinal ganglion cell responses. Comparison of the distance values from sham exposure with those from actual exposure yielded no significant differences. In addition, linear regression analysis of the distance values versus SAR values yielded no consistent dependence of light response changes. From these results we conclude that RF-EMF exposure at three mobile phone frequencies (GSM-900, GSM-1800, UMTS) and SARs up to 20 W/kg has no acute effects on retinal ganglion cell responses under constant temperature conditions.

(NE) Aït-Aïssa S, de Gannes FP, Taxile M, Billaudel B, Hurtier A, Haro E, Ruffié G, Athané A, Veyret B, Lagroye I. In Situ Expression of Heat-Shock Proteins and 3-Nitrotyrosine in Brains of Young Rats Exposed to a WiFi Signal In Utero and In Early Life. Radiat Res. 2013 May 10. [Epub ahead of print] (AS, CE, CH, DE, OX)

The bioeffects of exposure to Wireless High-Fidelity (WiFi) signals on the developing nervous systems of young rodents was investigated by assessing the in vivo and in situ expression levels of three stress markers: 3-Nitrotyrosine (3-NT), an oxidative stress marker and two heat-shock proteins (Hsp25 and Hsp70). These biomarkers were measured in the brains of young rats exposed to a 2450 MHz WiFi signal by immunohistochemistry. Pregnant rats were first exposed or sham exposed to WiFi from day 6 to day 21 of gestation. In addition three newborns per litter were further exposed up to 5 weeks old. Daily 2-h exposures were performed blind in a

reverberation chamber and whole-body specific absorption rate levels were 0, 0.08, 0.4 and 4 W/kg. 3-NT and stress protein expression was assayed in different areas of the hippocampus and cortex. No significant difference was observed among exposed and sham-exposed groups. These results suggest that repeated exposure to WiFi during gestation and early life has no deleterious effects on the brains of young rats.

(E) Akbari A, Jelodar G, Nazifi S. Vitamin C protects rat cerebellum and encephalon from oxidative stress following exposure to radiofrequency wave generated by a BTS antenna model. Toxicol Mech Methods. 24(5):347-352, 2014. (AS, CE, CH, OX, IA)

Radio frequency wave (RFW) generated by base transceiver station has been reported to produce deleterious effects on the central nervous system function, possibly through oxidative stress. This study was conducted to evaluate the effect of RFW-induced oxidative stress in the cerebellum and encephalon and the prophylactic effect of vitamin C on theses tissues by measuring the antioxidant enzymes activity, including: glutathione peroxidase, superoxide dismutase, catalase, and malondialdehyde (MDA). Thirty-two adult male Sprague-Dawley rats were randomly divided into four equal groups. The control group; the control-vitamin C group received L-ascorbic acid (200 mg/kg of body weight/day by gavage) for 45 days. The RFW group was exposed to RFW and the RFW+ vitamin C group was exposed to RFW and received vitamin C. At the end of the experiment, all groups were killed and encephalon and cerebellum of all rats were removed and stored at -70 °C for measurement of antioxidant enzymes activity and MDA. The results indicate that exposure to RFW in the test group decreased antioxidant enzymes activity and increased MDA compared with the control groups ($p < 0.05$). The protective role of vitamin C in the treated group improved antioxidant enzymes activity and reduced MDA compared with the test group ($p < 0.05$). It can be concluded that RFW causes oxidative stress in the brain and vitamin C improves the antioxidant enzymes activity and decreases MDA.

(E) Aldad TS, Gan G, Gao XB, Taylor HS. Fetal radiofrequency radiation exposure from 800-1900 MHz-rated cellular telephones affects neurodevelopment and behavior in mice. Sci Rep. 2:312, 2012. (AS, CS, DE, BE, CE, CC)

Neurobehavioral disorders are increasingly prevalent in children, however their etiology is not well understood. An association between prenatal cellular telephone use and hyperactivity in children has been postulated, yet the direct effects of radiofrequency radiation exposure on neurodevelopment remain unknown. Here we used a mouse model to demonstrate that in-utero radiofrequency exposure from cellular telephones does affect adult behavior. Mice exposed in-utero were hyperactive and had impaired memory as determined using the object recognition, light/dark box and step-down assays. Whole cell patch clamp recordings of miniature excitatory postsynaptic currents (mEPSCs) revealed that these behavioral changes were due to altered neuronal developmental programming. Exposed mice had dose-responsive impaired glutamatergic synaptic transmission onto layer V pyramidal neurons of the prefrontal cortex. We present the first experimental evidence of neuropathology due to in-utero cellular telephone radiation. Further experiments are needed in humans or non-human primates to determine the risk of exposure during pregnancy.

(E) Ammari M, Brillaud E, Gamez C, Lecomte A, Sakly M, Abdelmelek H, de Seze R. Effect of a chronic GSM 900 MHz exposure on glia in the rat brain. Biomed Pharmacother. 62(4):273-281, 2008a. (AS, CE, CC)

Extension of the mobile phone technology raises concern about the health effects of 900 MHz microwaves on the central nervous system (CNS). In this study we measured GFAP expression using immunocytochemistry method, to evaluate glial evolution 10 days after a chronic exposure (5 days a week for 24 weeks) to GSM signal for 45 min/day at a brain-averaged specific absorption rate (SAR)=1.5 W/kg and for 15 min/day at a SAR=6 W/kg in the following rat brain areas: prefrontal cortex (PfCx), caudate putamen (Cpu), lateral globus pallidus of striatum (LGP), dentate gyrus of hippocampus (DG) and cerebellum cortex (CCx). In comparison to sham or cage control animals, rats exposed to chronic GSM signal at 6 W/kg have increased GFAP stained surface areas in the brain ($p<0.05$). But the chronic exposure to GSM at 1.5 W/kg did not increase GFAP expression. Our results indicated that chronic exposure to GSM 900 MHz microwaves (SAR=6 W/kg) may induce persistent astroglia activation in the rat brain (sign of a potential gliosis).

(E) Ammari M, Lecomte A, Sakly M, Abdelmelek H, de-Seze R. Exposure to GSM 900 MHz electromagnetic fields affects cerebral cytochrome c oxidase activity. Toxicology. 250(1):70-74, 2008b. (AS, CE, CH)

The world-wide and rapidly growing use of mobile phones has raised serious concerns about the biological and health-related effects of radio frequency (RF) radiation, particularly concerns about the effects of RFs upon the nervous system. The goal of this study was conducted to measure cytochrome oxidase (CO) levels using histochemical methods in order to evaluate regional brain metabolic activity in rat brain after exposure to a GSM 900 MHz signal for 45 min/day at a brain-averaged specific absorption rate (SAR) of 1.5 W/Kg or for 15 min/day at a SAR of 6 W/Kg over seven days. Compared to the sham and control cage groups, rats exposed to a GSM signal at 6 W/Kg showed decreased CO activity in some areas of the prefrontal and frontal cortex (infralimbic cortex, prelimbic cortex, primary motor cortex, secondary motor cortex, anterior cingulate cortex areas 1 and 2 (Cg1 and Cg2)), the septum (dorsal and ventral parts of the lateral septal nucleus), the hippocampus (dorsal field CA1, CA2 and CA3 of the hippocampus and dental gyrus) and the posterior cortex (retrosplenial agranular cortex, primary and secondary visual cortex, perirhinal cortex and lateral entorhinal cortex). However, the exposure to GSM at 1.5 W/Kg did not affect brain activity. Our results indicate that 6 W/Kg GSM 900 MHz microwaves may affect brain metabolism and neuronal activity in rats.

(NE) Ammari M, Jacquet A, Lecomte A, Sakly M, Abdelmelek H, de Seze R. Effect of head-only sub-chronic and chronic exposure to 900-MHz GSM electromagnetic fields on spatial memory in rats. Brain Inj. 22(13-14):1021-1029, 2008c. (AS, CE, BE)

PRIMARY OBJECTIVE: This study was carried out to investigate the behavioural effects of sub-chronic and chronic head-only exposure to 900 MHz GSM (Global System for Mobile communications) in male rats. **METHODS:** Rats were exposed for 45 minutes per day, at a

brain-averaged specific absorption rate (SAR) = 1.5 W Kg(-1) or 15 minutes per day at a SAR = 6 W Kg(-1), during 8 or 24 weeks. Then, their spatial memory was tested using the radial-arm maze. In the first phase (10 days), rats were trained to visit the eight arms of the maze without returning to an arm already visited. In the second phase (8 days), a 45-minute intra-trial delay was introduced after four visited arms. **RESULTS:** Performance of exposed rats (1.5 or 6 W Kg(-1)) was compared with that of sham, negative control and positive control rats. Scopolamine treatment in the positive control rats induced deficit in spatial memory task in the second phase of the test. However, spatial memory task was unaffected in exposed rats. **CONCLUSION:** Sub-chronic and chronic head-only exposure of rats to GSM 900 MHz signal (45-minutes, SAR = 1.5 or 15-minutes, SAR = 6 W Kg(-1)) did not induce spatial memory deficit in the radial-arm maze.

(E) Ammari M, Gamez C, Lecomte A, Sakly M, Abdelmelek H, De Seze R. GFAP expression in the rat brain following sub-chronic exposure to a 900 MHz electromagnetic field signal. Int J Radiat Biol. 86(5):367-375, 2010. (AS, CE, CC)

PURPOSE: The rapid development and expansion of mobile communications contributes to the general debate on the effects of electromagnetic fields emitted by mobile phones on the nervous system. This study aims at measuring the glial fibrillary acidic protein (GFAP) expression in 48 rat brains to evaluate reactive astrocytosis, three and 10 days after long-term head-only sub-chronic exposure to a 900 MHz electromagnetic field (EMF) signal, in male rats. **METHODS:** Sprague-Dawley rats were exposed for 45 min/day at a brain-averaged specific absorption rate (SAR) = 1.5 W/kg or 15 min/day at a SAR = 6 W/kg for five days per week during an eight-week period. GFAP expression was measured by the immunocytochemistry method in the following rat brain areas: Prefrontal cortex, cerebellar cortex, dentate gyrus of the hippocampus, lateral globus pallidus of the striatum, and the caudate putamen. **RESULTS:** Compared to the sham-treated rats, those exposed to the sub-chronic GSM (Global System for mobile communications) signal at 1.5 or 6 W/kg showed an increase in GFAP levels in the different brain areas, three and ten days after treatment. **CONCLUSION:** Our results show that sub-chronic exposures to a 900 MHz EMF signal for two months could adversely affect rat brain (sign of a potential gliosis).

(E) Arendash GW, Sanchez-Ramos J, Mori T, Mamcarz M, Lin X, Runfeldt M, Wang L, Zhang G, Sava V, Tan J, Cao C. Electromagnetic field treatment protects against and reverses cognitive impairment in Alzheimer's disease mice. J Alzheimers Dis. 19(1):191-210, 2010. (AS, CE, CH, BE, MA)

Despite numerous studies, there is no definitive evidence that high-frequency electromagnetic field (EMF) exposure is a risk to human health. To the contrary, this report presents the first evidence that long-term EMF exposure directly associated with cell phone use (918 MHz; 0.25 w/kg) provides cognitive benefits. Both cognitive-protective and cognitive-enhancing effects of EMF exposure were discovered for both normal mice and transgenic mice destined to develop Alzheimer's-like cognitive impairment. The cognitive interference task utilized in this study was designed from, and measure-for-measure analogous to, a human cognitive interference task. In

Alzheimer's disease mice, long-term EMF exposure reduced brain amyloid-beta (Abeta) deposition through Abeta anti-aggregation actions and increased brain temperature during exposure periods. Several inter-related mechanisms of EMF action are proposed, including increased Abeta clearance from the brains of Alzheimer's disease mice, increased neuronal activity, and increased cerebral blood flow. Although caution should be taken in extrapolating these mouse studies to humans, we conclude that EMF exposure may represent a non-invasive, non-pharmacologic therapeutic against Alzheimer's disease and an effective memory-enhancing approach in general.

(E) Arendash GW, Mori T, Dorsey M, Gonzalez R, Tajiri N, Borlongan C. Electromagnetic treatment to old Alzheimer's mice reverses β-amyloid deposition, modifies cerebral blood flow, and provides selected cognitive benefit. PLoS One. 7(4):e35751, 2012. (AS, CE, CH, BE, MA)

Few studies have investigated physiologic and cognitive effects of "long-term" electromagnetic field (EMF) exposure in humans or animals. Our recent studies have provided initial insight into the long-term impact of adulthood EMF exposure (GSM, pulsed/modulated, 918 MHz, 0.25-1.05 W/kg) by showing 6+ months of daily EMF treatment protects against or reverses cognitive impairment in Alzheimer's transgenic (Tg) mice, while even having cognitive benefit to normal mice. Mechanistically, EMF-induced cognitive benefits involve suppression of brain β-amyloid (Aβ) aggregation/deposition in Tg mice and brain mitochondrial enhancement in both Tg and normal mice. The present study extends this work by showing that daily EMF treatment given to very old (21-27 month) Tg mice over a 2-month period reverses their very advanced brain Aβ aggregation/deposition. These very old Tg mice and their normal littermates together showed an increase in general memory function in the Y-maze task, although not in more complex tasks. Measurement of both body and brain temperature at intervals during the 2-month EMF treatment, as well as in a separate group of Tg mice during a 12-day treatment period, revealed no appreciable increases in brain temperature (and no/slight increases in body temperature) during EMF "ON" periods. Thus, the neuropathologic/cognitive benefits of EMF treatment occur without brain hyperthermia. Finally, regional cerebral blood flow in cerebral cortex was determined to be reduced in both Tg and normal mice after 2 months of EMF treatment, most probably through cerebrovascular constriction induced by freed/disaggregated Aβ (Tg mice) and slight body hyperthermia during "ON" periods. These results demonstrate that long-term EMF treatment can provide general cognitive benefit to very old Alzheimer's Tg mice and normal mice, as well as reversal of advanced Aβ neuropathology in Tg mice without brain heating. Results further underscore the potential for EMF treatment against AD.

***(E) Arns M, Van Luijtelaar G, Sumich A, Hamilton R, Gordon E. Electroencephalographic, personality, and executive function measures associated with frequent mobile phone use. Int J Neurosci. 117(9):1341-1360, 2007. (HU, BE) (*Effects observed probably not caused by exposure to RFR.)**

The present study employs standardized data acquired from the Brain Resource International Database to study the relationship between mobile phone usage, personality, and brain

function (n = 300). Based on the frequency and duration of mobile phone usage, three groups were formed. The findings suggest a subtle slowing of brain activity related to mobile phone use that is not explained by differences in personality. These changes are still within normal physiological ranges. Better executive function in mobile phone users may reflect more focused attention, possibly associated with a cognitive training effect (i.e., frequently making phone calls in distracting places), rather than a direct effect of mobile phone use on cognition.

(E) Bak M, Dudarewicz A, Zmyślony M, Sliwinska-Kowalska M. Effects of GSM signals during exposure to event related potentials (ERPs). Int J Occup Med Environ Health. 23(2):191-199, 2010. (HU, EE)

OBJECTIVES: The primary aim of this work was to assess the effect of electromagnetic field (EMF) from the GSM mobile phone system on human brain function. The assessment was based on the assay of event related potentials (ERPs). **MATERIAL AND METHODS:** The study group consisted of 15 volunteers, including 7 men and 8 women. The test protocol comprised determination of P300 wave in each volunteer during exposure to the EMF. To eliminate possible effects of the applied test procedure on the final result, the test was repeated without EMF exposure. P300 latency, amplitude, and latency of the N1, N2, P2 waves were analysed. **RESULTS:** The statistical analysis revealed an effect of EMF on P300 amplitude. In the experiment with EMF exposure, lower P300 amplitudes were observed only at the time in which the volunteers were exposed to EMF; when the exposure was discontinued, the values of the amplitude were the same as those observed before EMF application. No such change was observed when the experiment was repeated with sham exposure, which may be considered as an indirect proof that lower P300 amplitude values were due to EMF exposure. No statistically significant changes were noted in the latencies of the N1, N2, P2 waves that precede the P300 wave, nor in the latency of the P300 itself. **CONCLUSIONS:** The results suggest that exposure to GSM EMF exerts some effects on CNS, including effects on long latency ERPs.

(E) Banaceur S, Banasr S, Sakly M, Abdelmelek H. Whole body exposure to 2.4 GHz WIFI signals: effects on cognitive impairment in adult triple transgenic mouse models of Alzheimer's disease (3xTg-AD). Behav Brain Res. 240:197-201, 2013. (AS, CE, BE, MA)

The present investigation aimed at evaluating the effects of long-term exposure to WIFI type radiofrequency (RF) signals (2.40 GHz), two hours per day during one month at a Specific Absorption Rate (SAR) of 1.60 W/kg. The effects of RF exposure were studied on wildtype mice and triple transgenic mice (3xTg-AD) destined to develop Alzheimer's-like cognitive impairment. Mice were divided into four groups: two sham groups (WT, TG; n=7) and two exposed groups (WTS, TGS; n=7). The cognitive interference task used in this study was designed from an analogous human cognitive interference task including the Flex field activity system test, the two-compartment box test and the Barnes maze test. Our data demonstrate for the first time that RF improves cognitive behavior of 3xTg-AD mice. We conclude that RF exposure may represent an effective memory-enhancing approach in Alzheimer's disease.

(E) Barcal J, Vozeh F. Effect of whole-body exposure to high-frequency electromagnetic field on the brain cortical and hippocampal activity in mouse experimental model. NeuroQuantology 5:292-302, 2007. (AS, EE)

Evaluation of the direct registration of brain cortical and hippocampal activity during a high-frequency electromagnetic field (HF-EMF) exposure was performed. Experimental procedures were done under general anesthesia (urethane, 20%, 2g/kg i.p.) in Lurcher mutant mice, wild type (healthy littermates) were used as controls. Animals were exposed to the HF-EMF with frequency corresponding to cellular phones (900 MHz). We used of gel electrodes (silicon tubes or glass microcapillary filled with agar) where the connection with classical electrodes was located out of HF-EMF space. ECoG evaluation showed a distinct shift to lower frequency components but clear effect has been observed only in wild type (healthy) mice whereas in Lurcher mutant mice only gentle differences between frequency spectra were found. Measurement of hippocampal rhythmicity showed gentle changes with increase of higher frequencies (i.e. opposite effect than in cortex) and changes in theta oscillations registered from a dentate gyrus and CA1 area in both types of animals (healthy and mutant). These findings support an idea about possible influencing the central nervous system by HF-EMF exposure and support also some recent results about possible health risks resulting from cellular phones use.

(E) Barthélémy A, Mouchard A, Bouji M, Blazy K, Puigsegur R, Villégier AS. Glial markers and emotional memory in rats following acute cerebral radiofrequency exposures. Environ Sci Pollut Res Int. 2016 Sep 30. [Epub ahead of print] (AS, BE, CE, CH)

The widespread mobile phone use raises concerns on the possible cerebral effects of radiofrequency electromagnetic fields (RF EMF). Reactive astrogliosis was reported in neuroanatomical structures of adaptive behaviors after a single RF EMF exposure at high specific absorption rate (SAR, 6 W/kg). Here, we aimed to assess if neuronal injury and functional impairments were related to high SAR-induced astrogliosis. In addition, the level of beta amyloid 1-40 (Aβ 1-40) peptide was explored as a possible toxicity marker. Sprague Dawley male rats were exposed for 15 min at 0, 1.5, or 6 W/kg or for 45 min at 6 W/kg. Memory, emotionality, and locomotion were tested in the fear conditioning, the elevated plus maze, and the open field. Glial fibrillary acidic protein (GFAP, total and cytosolic fractions), myelin basic protein (MBP), and Aβ1-40 were quantified in six brain areas using enzyme-linked immunosorbent assay. According to our data, total GFAP was increased in the striatum (+114 %) at 1.5 W/kg. Long-term memory was reduced, and cytosolic GFAP was increased in the hippocampus (+119 %) and in the olfactory bulb (+46 %) at 6 W/kg (15 min). No MBP or Aβ1-40 expression modification was shown. Our data corroborates previous studies indicating RF EMF-induced astrogliosis. This study suggests that RF EMF-induced astrogliosis had functional consequences on memory but did not demonstrate that it was secondary to neuronal damage.

(E) Bas O, Odaci E, Kaplan S, Acer N, Ucok K, Colakoglu S. 900 MHz electromagnetic field exposure affects qualitative and quantitative features of hippocampal pyramidal cells in the adult female rat. Brain Res. 1265:178-185, 2009. (AS, CE, ME)

The effects of electromagnetic fields (EMFs) emitted by mobile phones on humans hold special interest due to their use in close proximity to the brain. The current study investigated the number of pyramidal cells in the cornu ammonis (CA) of the 16-week-old female rat hippocampus following postnatal exposure to a 900 megahertz (MHz) EMF. In this study were three groups of 6 rats: control (Cont), sham exposed (Sham), and EMF exposed (EMF). EMF group rats were exposed to 900 MHz EMF (1 h/day for 28 days) in an exposure tube. Sham group was placed in the exposure tube but not exposed to EMF (1 h/day for 28 days). Cont group was not placed into the exposure tube nor were they exposed to EMF during the study period. In EMF group rats, the specific energy absorption rate (SAR) varied between 0.016 (whole body) and 2 W/kg (locally in the head). All of the rats were sacrificed at the end of the experiment and the number of pyramidal cells in the CA was estimated using the optical fractionator technique. Histopathological evaluations were made on sections of the CA region of the hippocampus. Results showed that postnatal EMF exposure caused a significant decrease of the pyramidal cell number in the CA of the EMF group ($P<0.05$). Additionally, cell loss can be seen in the CA region of EMF group even at qualitative observation. These results may encourage researchers to evaluate the chronic effects of 900 MHz EMF on teenagers' brains.

(E) Baş O, Sönmez OF, Aslan A, İkinci A, Hancı H, Yıldırım M, Kaya H, Akça M, Odacı E. Pyramidal Cell Loss in the Cornu Ammonis of 32-day-old Female Rats Following Exposure to a 900 Megahertz Electromagnetic Field During Prenatal Days 13–21. NeuroQuantology 11:591-599, 2013. (AS, CE, ME, DE)

The number of studies reporting that the electromagnetic field (EMF) emitted by mobile phones affects human health is increasing by the day. In previous studies we reported that a 900 megahertz (MHz) EMF applied throughout the prenatal period reduced the number of pyramidal cells in the cornu ammonis of rat pups in the postnatal period. In this study we investigated the effect of a 900 MHz EMF applied on days 13-21 of the prenatal period on the number of pyramidal cells in the cornu ammonis of rat pups in the postnatal period. For that purpose, pregnant rats were divided into experimental and control groups. Experimental group pregnant rats were exposed to the effect of a 900 MHz EMF on days 13-21 of pregnancy. No procedure was applied to the control group. Newborn female rat pups were added to the study, and no procedure was performed on these after birth. Five newborn female rats were obtained from the experimental group and six from the control group. All female rat pups were decapitated on the postnatal 32nd day, and histological procedures were performed on the brain tissues. Sections were stained with Cresyl fast violet. The optical dissector technique was used to estimate the total number of pyramidal cells in the cornu ammonis. Sections of cornu ammonis were subjected to histopathological evaluations. Our results showed that exposure to 900 MHz EMF during prenatal days 13-21 led to a significant decrease in the number of pyramidal cells in the cornu ammonis of the experimental group female rat pups ($P<0.05$). Histopathological examination revealed picnotic cells in the cornu ammonis in experimental

female rat pups. The pyramidal cell loss in the cornu ammonis may therefore be attributed to exposure to 900 MHz EMF in days 13-21 of the prenatal period.

(NE) Bhagat S, Varshney S, Bist SS, Goel D, Mishra S, Jha VK. Effects on auditory function of chronic exposure to electromagnetic fields from mobile phones. Ear Nose Throat J. 95(8):E18-22, 2016. (HU, PE)

The widespread use of mobile phones has given rise to apprehension regarding the possible hazardous health effects of high-frequency electromagnetic fields (EMFs) on auditory function. We conducted a study to investigate the effects of long-term (>4 yr) exposure to EMFs emitted by mobile phones on auditory function. Our study population was made up of 40 healthy medical students-31 men and 9 women, aged 20 to 30 years (mean 22.7). Of this group, 31 subjects typically held their phone to the right ear and 9 to the left ear; the non-phone-using ear served as each subject's control ear. The phone-using subjects were also split into two groups of 20 based on the duration of their daily phone use (≤60 min vs. >60 min). All subjects underwent pure-tone audiometry, speech audiometry, impedance audiometry, and brainstem evoked response audiometry (BERA), and comparisons were made between the phone-using ear and the control ear and between the shorter and longer duration of daily use. We found no statistically significant differences in high-frequency pure-tone average between the phone-using ears and the control ears ($p = 0.69$) or between the shorter- and longer-duration phone-using ears ($p = 0.85$). Moreover, statistical analysis of BERA findings revealed no significant differences between the phone-using ears and the control ears in terms of wave I-III, III-V, and I-V interpeak latencies ($p = 0.59$, 0.74 and 0.44, respectively). None of the subjects reported any subjective symptoms, such as headache, tinnitus, or sensations of burning or warmth behind, around, or on the phone-using ear. We conclude that the long-term exposure to EMFs from mobile phones does not affect auditory function.

(E) Bodera P, Stankiewicz W, Antkowiak B, Paluch M, Kieliszek J, Sobiech J, Zdanowski R, Wojdas A, Siwicki AK, Skopińska-Rózewska E. Suppressive effect of electromagnetic field on analgesic activity of tramadol in rats. Pol J Vet Sci. 15(1):95-100, 2012. (AS, PE, IA)

The electromagnetic fields (EMFs) have been shown to alter animal and human behavior, such as directional orientation, learning, pain perception (nociception or analgesia) and anxiety-related behaviors. The aim of this study was to evaluate the influence of electromagnetic fields of high-frequency microwaves on pain perception and anti-nociceptive activity of tramadol (TRAM) - analgetic effective in the treatment of moderate to severe acute and chronic pain states. Electromagnetic fields exposures of a)1500 MHz frequency and b) modulated, 1800 MHz (which is identical to that generated by mobile phones) were applied. Paw withdrawal latency (PWL) to thermal stimulus was measured in vehicle or tramadol (TRAM) treated animals before and after 30, 60 and 90 minutes from injections. The differences in the level of pain (PWL) between control group and rats exposed to EMF alone in three measurements, were not observed. Tramadol alone significantly increased PWLs to thermal stimulus in comparison to vehicle results at 30 ($p < 0.001$) and 60 minutes ($p < 0.05$) after drug injection. EMF exposure of both frequencies transiently suppressed analgesic effect of tramadol, significantly reducing paw withdrawal latency in animals treated with this drug at 30 minutes from the drug injection.

(E) Bodera P, Stankiewicz W, Antkowiak B, Paluch M, Kieliszek J, Sobiech J, Niemcewicz M. Influence of electromagnetic field (1800 MHz) on lipid peroxidation in brain, blood, liver and kidney in rats. Int J Occup Med Environ Health. 28(4):751-759, 2015. (AS, OX)

OBJECTIVES: The aim of this study is the evaluation of the influence of repeated (5 times for 15 min) exposure to electromagnetic field (EMF) of 1800 MHz frequency on tissue lipid peroxidation (LPO) both in normal and inflammatory state, combined with analgesic treatment. MATERIAL AND METHODS: The concentration of malondialdehyde (MDA) as the end-product of the lipid peroxidation (LPO) was estimated in blood, liver, kidneys, and brain of Wistar rats, both healthy and those with complete Freund's adjuvant (CFA)-induced persistent paw inflammation. RESULTS: The slightly elevated levels of the MDA in blood, kidney, and brain were observed among healthy rats in electromagnetic field (EMF)-exposed groups, treated with tramadol (TRAM/EMF and exposed to the EMF). The malondialdehyde remained at the same level in the liver in all investigated groups: the control group (CON), the exposed group (EMF), treated with tramadol (TRAM) as well as exposed to and treated with tramadol (TRAM/EMF). In the group of animals treated with the complete Freund's adjuvant (CFA) we also observed slightly increased values of the MDA in the case of the control group (CON) and the exposed groups (EMF and TRAM/EMF). The MDA values concerning kidneys remained at the same levels in the control, exposed, and not-exposed group treated with tramadol. Results for healthy rats and animals with inflammation did not differ significantly. CONCLUSIONS: The electromagnetic field exposure (EMF), applied in the repeated manner together with opioid drug tramadol (TRAM), slightly enhanced lipid peroxidation level in brain, blood, and kidneys.

(E) Bouji M, Lecomte A, Hode Y, de Seze R, Villégier AS. Effects of 900 MHz radiofrequency on corticosterone, emotional memory and neuroinflammation in middle-aged rats. Exp Gerontol. 47(6):444-451, 2012. (AS, CC, BE, AD)

The widespread use of mobile phones raises the question of the effects of electromagnetic fields (EMF, 900 MHz) on the brain. Previous studies reported increased levels of the glial fibrillary acidic protein (GFAP) in the rat's brain after a single exposure to 900 MHz global system for mobile (GSM) signal, suggesting a potential inflammatory process. While this result was obtained in adult rats, no data is currently available in older animals. Since the transition from middle-age to senescence is highly dependent on environment and lifestyle, we studied the reactivity of middle-aged brains to EMF exposure. We assessed the effects of a single 15 min GSM exposure (900 MHz; specific absorption rate (SAR)=6 W/kg) on GFAP expression in young adults (6 week-old) and middle-aged rats (12 month-old). Brain interleukin (IL)-1β and IL-6, plasmatic levels of corticosterone (CORT), and emotional memory were also assessed. Our data indicated that, in contrast to previously published work, acute GSM exposure did not induce astrocyte activation. Our results showed an IL-1β increase in the olfactory bulb and enhanced contextual emotional memory in GSM-exposed middle-aged rats, and increased plasmatic levels of CORT in GSM-exposed young adults. Altogether, our data showed an age dependency of reactivity to GSM exposure in neuro-immunity, stress and behavioral

parameters. Reproducing these effects and studying their mechanisms may allow a better understanding of mobile phone EMF effects on neurobiological parameters.

(E) Brillaud E, Piotrowski A, de Seze R. Effect of an acute 900 MHz GSM exposure on glia in the rat brain: a time-dependent study. Toxicology. 238(1):23-33, 2007. (AS, CC)

Because of the increasing use of mobile phones, the possible risks of radio frequency electromagnetic fields adverse effects on the human brain has to be evaluated. In this work we measured GFAP expression, to evaluate glial evolution 2, 3, 6 and 10 days after a single GSM exposure (15min, brain averaged SAR=6W/kg, 900 MHz signal) in the rat brain. A statistically significant increase of GFAP stained surface area was observed 2 days after exposure in the frontal cortex and the caudate putamen. A smaller statistically significant increase was noted 3 days after exposure in the same areas and in the cerebellum cortex. Our results confirm the Mausset-Bonnefont et al. study [Mausset-Bonnefont, A.L., Hirbec, H., Bonnefont, X., Privat, A., Vignon, J., de Seze, R., 2004. Acute exposure to GSM 900MHz electromagnetic fields induces glial reactivity and biochemical modifications in the rat brain. Neurobiol. Dis. 17, 445-454], showing the existence of glial reactivity after a 15min GSM acute exposure at a brain averaged SAR of 6W/kg. We conclude to a temporary effect, probably due to a hypertrophy of glial cells, with a temporal and a spatial modulation of the effect. Whether this effect could be harmful remains to be studied.

(E) Calabrò E, Condello S, Currò M, Ferlazzo N, Caccamo D, Magazù S, Ientile R. Modulation of heat shock protein response in SH-SY5Y by mobile phone microwaves. World J Biol Chem. 3(2):34-40, 2012. (CS, CH)

AIM: To investigate putative biological damage caused by GSM mobile phone frequencies by assessing electromagnetic fields during mobile phone working. METHODS: Neuron-like cells, obtained by retinoic-acid-induced differentiation of human neuroblastoma SH-SY5Y cells, were exposed for 2 h and 4 h to microwaves at 1800 MHz frequency bands. RESULTS: Cell stress response was evaluated by MTT assay as well as changes in the heat shock protein expression (Hsp20, Hsp27 and Hsp70) and caspase-3 activity levels, as biomarkers of apoptotic pathway. Under our experimental conditions, neither cell viability nor Hsp27 expression nor caspase-3 activity was significantly changed. Interestingly, a significant decrease in Hsp20 expression was observed at both times of exposure, whereas Hsp70 levels were significantly increased only after 4 h exposure. CONCLUSION: The modulation of the expression of Hsps in neuronal cells can be an early response to radiofrequency microwaves.

(NE) Calvente I, Pérez-Lobato R, Núñez MI, Ramos R, Guxens M, Villalba J, Olea N, Fernández MF. Does exposure to environmental radiofrequency electromagnetic fields cause cognitive and behavioral effects in 10-year-old boys? Bioelectromagnetics. 37(1):25-36, 2016. (HU, BE)

The relationship between exposure to electromagnetic fields from non-ionizing radiation and adverse human health effects remains controversial. We aimed to explore the association of environmental radiofrequency-electromagnetic fields (RF-EMFs) exposure with neurobehavioral function of children. A subsample of 123 boys belonging to the Environment

and Childhood cohort from Granada (Spain), recruited at birth from 2000 through 2002, were evaluated at the age of 9-11 years. Spot electric field measurements within the 100 kHz to 6 GHz frequency range, expressed as both root mean-square (SRMS) and maximum power density (SMAX) magnitudes, were performed in the immediate surrounds of childreńs dwellings. Neurocognitive and behavioral functions were assessed with a comprehensive battery of tests. Multivariate linear and logistic regression models were used, adjusting for potential confounders. All measurements were lower than reference guideline limits, with median SRMS and SMAX values of 285.94 and 2759.68 µW/m(2) , respectively. Most of the cognitive and behavioral parameters did not show any effect, but children living in higher RF exposure areas (above median SRMS levels) had lower scores for verbal expression/comprehension and higher scores for internalizing and total problems, and obsessive-compulsive and post-traumatic stress disorders, in comparison to those living in areas with lower exposure. These associations were stronger when SMAX values were considered. Although some of our results may suggest that low-level environmental RF-EMF exposure has a negative impact on cognitive and/or behavior development in children; given limitations in the study design and that the majority of neurobehavioral functioning tasks were not affected, definitive conclusions cannot be drawn.

(E) Cammaerts MC, De Doncker P, Patris X, Bellens F, Rachidi Z, Cammaerts D. GSM 900 MHz radiation inhibits ants' association between food sites and encountered cues. Electromagn Biol Med. 31(2):151-165, 2012. (AS, BE)

The kinetics of the acquisition and loss of the use of olfactory and visual cues were previously obtained in six experimental colonies of the ant Myrmica sabuleti meinert 1861, under normal conditions. In the present work, the same experiments were conducted on six other naive identical colonies of M. sabuleti, under electromagnetic radiation similar to those surrounding GSM and communication masts. In this situation, no association between food and either olfactory or visual cues occurred. After a recovery period, the ants were able to make such an association but never reached the expected score. Such ants having acquired a weaker olfactory or visual score and still undergoing olfactory or visual training were again submitted to electromagnetic waves. Not only did they lose all that they had memorized, but also they lost it in a few hours instead of in a few days (as under normal conditions when no longer trained). They kept no visual memory at all (instead of keeping 10% of it as they normally do). The impact of GSM 900 MHz radiation was greater on the visual memory than on the olfactory one. These communication waves may have such a disastrous impact on a wide range of insects using olfactory and/or visual memory, i.e., on bees.

(E) Cammaerts MC, Rachidi Z, Bellens F, De Doncker P. Food collection and response to pheromones in an ant species exposed to electromagnetic radiation. Electromagn Biol Med. 2013 Jan 15. [Epub ahead of print] (AS, BE)

We used the ant species Myrmica sabuleti as a model to study the impact of electromagnetic waves on social insects' response to their pheromones and their food collection. We quantified M. sabuleti workers' response to their trail, area marking and alarm pheromone under normal

conditions. Then, we quantified the same responses while under the influence of electromagnetic waves. Under such an influence, ants followed trails for only short distances, no longer arrived at marked areas and no longer orientated themselves to a source of alarm pheromone. Also when exposed to electromagnetic waves, ants became unable to return to their nest and recruit congeners; therefore, the number of ants collecting food increases only slightly and slowly. After 180 h of exposure, their colonies deteriorated. Electromagnetic radiation obviously affects social insects' behavior and physiology.

(E) Cammaerts M-C, Vandenbosch GAE, Volski V. Effect of short-term GSM radiation at representative levels in society on a biological model: the ant Myrmica sabuleti. J Insect Beh. 27(4):514-526. 2014. (AS, CE, BE)

Well-controlled electromagnetic exposure conditions were set up at a representative societal GSM radiation intensity level, 1.5 V/m, which is the legally allowed level in Brussels. Two nests of the ant species Myrmica sabuleti were repeatedly irradiated during 10 min. before their behavior was observed, based on the analysis of the ant trajectories. Under these exposure conditions, behavioral effects were detected. The ants' locomotion slightly changed. The ants' orientation towards their attractive alarm pheromone statistically became of lower quality. The ants still presented their trail following behavior but less efficiently. In this controversial issue, ants could be considered as possible bioindicators.

(E) Carballo-Quintás M, Martínez-Silva I, Cadarso-Suárez C, Alvarez-Figueiras M, Ares-Pena FJ, López-Martín E. A study of neurotoxic biomarkers, c-fos and GFAP after acute exposure to GSM radiation at 900 MHz in the picrotoxin model of rat brains. Neurotoxicology. 32(4):478-494, 2011. (AS, CH)

The acute effects of microwave exposure from the Global System for Mobile Communication (GSM) were studied in rats, using 900 MHz radiation at an intensity similar to mobile phone emissions. Acute subconvulsive doses of picrotoxin were then administered to the rats and an experimental model of seizure-proneness was created from the data. Seventy-two adult male Sprague-Dawley rats underwent immunochemical testing of relevant anatomical areas to measure induction of the c-fos neuronal marker after 90min and 24h, and of the glial fibrillary acidic protein (GFAP) 72h after acute exposure to a 900MHz electromagnetic field (EMF). The experimental set-up facilitated measurement of absorbed power, from which the average specific absorption rate was calculated using the finite-difference time-domain (FDTD) 2h after exposure to EMF radiation at 1.45W/kg in picrotoxin-treated rats and 1.38W/kg in untreated rats. Ninety minutes after radiation high levels of c-fos expression were recorded in the neocortex and paleocortex along with low hippocampus activation in picrotoxin treated animals. Most brain areas, except the limbic cortical region, showed important increases in neuronal activation 24h after picrotoxin and radiation. Three days after picrotoxin treatment, radiation effects were still apparent in the neocortex, dentate gyrus and CA3, but a significant decrease in activity was noted in the piriform and entorhinal cortex. During this time, glial

reactivity increased with every seizure in irradiated, picrotoxin-treated brain regions. Our results reveal that c-fos and glial markers were triggered by the combined stress of non-thermal irradiation and the toxic effect of picrotoxin on cerebral tissues.

(E) Çeliker M, Özgür A, Tümkaya L, Terzi S, Yılmaz M, Kalkan Y, Erdoğan E. Effects of exposure to 2100MHz GSM-like radiofrequency electromagnetic field on auditory system of rats. Braz J Otorhinolaryngol. 2016 Nov 5. pii: S1808-8694(16)30222-1. doi: 10.1016/j.bjorl.2016.10.004. [Epub ahead of print] (AS, CE, CC, EE)

INTRODUCTION: The use of mobile phones has become widespread in recent years. Although beneficial from the communication viewpoint, the electromagnetic fields (EMF) generated by mobile phones may cause unwanted biological changes in the human body. OBJECTIVE: In this study, we aimed to evaluate the effects of 2100MHz Global System for Mobile communication (GSM-like) electromagnetic field (EMF), generated by an EMF generator, on the auditory system of rats by using electrophysiological, histopathologic and immunohistochemical methods. METHODS: Fourteen adult Wistar albino rats were included in the study. The rats were divided randomly into two groups of seven rats each. The study group was exposed continuously for 30 days to a 2100MHz EMF with a signal level (power) of 5.4dBm (3.47mW) to simulate the talk mode on a mobile phone. The control group was not exposed to the aforementioned EMF. After 30days, the Auditory Brainstem Responses (ABRs) of both groups were recorded and the rats were sacrificed. The cochlear nuclei were evaluated by histopathologic and immunohistochemical methods. RESULTS: The ABR records of the two groups did not differ significantly. The histopathologic analysis showed increased degeneration signs in the study group (p=0.007). In addition, immunohistochemical analysis revealed increased apoptotic index in the study group compared to that in the control group (p=0.002). CONCLUSION: The results support that long-term exposure to a GSM-like 2100MHz EMF causes an increase in neuronal degeneration and apoptosis in the auditory system.

(E) Cetin H, Nazıroğlu M, Celik O, Yüksel M, Pastacı N, Ozkaya MO. Liver antioxidant stores protect the brain from electromagnetic radiation (900 and 1800 MHz)-induced oxidative stress in rats during pregnancy and the development of offspring. J Matern Fetal Neonatal Med. 2014 Mar 3. [Epub ahead of print] (AS, CE, CH, OX, DE)

Objectives: The present study determined the effects of mobile phone (900 and 1800 MHz)-induced electromagnetic radiation (EMR) exposure on oxidative stress in the brain and liver as well as the element levels in growing rats from pregnancy to 6 weeks of age. Methods: Thirty-two rats and their offspring were equally divided into 3 different groups: the control, 900 MHz, and 1800 MHz groups. The 900 MHz and 1800 MHz groups were exposed to EMR for 60 min/day during pregnancy and neonatal development. At the 4th, 5th, and 6th weeks of the experiment, brain samples were obtained. Results: Brain and liver glutathione peroxidase (GSH-Px) activities, as well as liver vitamin A and β-carotene concentrations decreased in the EMR groups, although brain iron, vitamin A, and β-carotene concentrations increased in the EMR groups. In the 6th week, selenium concentrations in the brain decreased in the EMR

groups. There were no statistically significant differences in glutathione, vitamin E, chromium, copper, magnesium, manganese, and zinc concentrations between the 3 groups. Conclusion: EMR-induced oxidative stress in the brain and liver was reduced during the development of offspring. Mobile phone-induced EMR could be considered as a cause of oxidative brain and liver injury in growing rats.

(E) Chen C, Ma Q, Liu C, Deng P, Zhu G, Zhang L, He M, Lu Y, Duan W, Pei L, Li M, Yu Z, Zhou Z. Exposure to 1800 MHz radiofrequency radiation impairs neurite outgrowth of embryonic neural stem cells. Sci Rep. 2014 May 29;4:5103. doi: 10.1038/srep05103. (CS, ME, DE)

A radiofrequency electromagnetic field (RF-EMF) of 1800 MHz is widely used in mobile communications. However, the effects of RF-EMFs on cell biology are unclear. Embryonic neural stem cells (eNSCs) play a critical role in brain development. Thus, detecting the effects of RF-EMF on eNSCs is important for exploring the effects of RF-EMF on brain development. Here, we exposed eNSCs to 1800 MHz RF-EMF at specific absorption rate (SAR) values of 1, 2, and 4 W/kg for 1, 2, and 3 days. We found that 1800 MHz RF-EMF exposure did not influence eNSC apoptosis, proliferation, cell cycle or the mRNA expressions of related genes. RF-EMF exposure also did not alter the ratio of eNSC differentiated neurons and astrocytes. However, neurite outgrowth of eNSC differentiated neurons was inhibited after 4 W/kg RF-EMF exposure for 3 days. Additionally, the mRNA and protein expression of the proneural genes Ngn1 and NeuroD, which are crucial for neurite outgrowth, were decreased after RF-EMF exposure. The expression of their inhibitor Hes1 was upregulated by RF-EMF exposure. These results together suggested that 1800 MHz RF-EMF exposure impairs neurite outgrowth of eNSCs. More attention should be given to the potential adverse effects of RF-EMF exposure on brain development.

(E) Choi Y-J, Choi Y-S. Effects of Electromagnetic Radiation from Smartphones on Learning Ability and Hippocampal Progenitor Cell Proliferation in Mice. Osong Public Health and Research Perspectives. 7(1):12-17, 2016. (AS, CE, CC, BE)

Objectives Nonionizing radiation is emitted from electronic devices, such as smartphones. In this study, we intended to elucidate the effect of electromagnetic radiation from smartphones on spatial working memory and progenitor cell proliferation in the hippocampus. Methods Both male and female mice were randomly separated into two groups (radiated and control) and the radiated group was exposed to electromagnetic radiation for 9 weeks and 11 weeks for male and female mice, respectively. Spatial working memory was examined with a Y maze, and proliferation of hippocampal progenitor cells were examined by 5-bromo-2'-deoxyuridine administration and immunohistochemical detection. Results When spatial working memory on a Y maze was examined in the 9th week, there was no significant difference in the spontaneous alternation score on the Y maze between the two groups. In addition, there was no significant difference in hippocampal progenitor cell proliferation. However, immunoreactivity to glial fibrillary acidic protein was increased in exposed animals. Next, to test the effect of recovery following chronic radiation exposure, the remaining female mice were further exposed to

electromagnetic radiation for 2 more weeks (total 11 weeks), and spontaneous alternation was tested 4 weeks later. In this experiment, although there was no significant difference in the spontaneous alternation scores, the number of arm entry was significantly increased. Conclusion These data indicate that although chronic electromagnetic radiation does not affect spatial working memory and hippocampal progenitor cell proliferation it can mediate astrocyte activation in the hippocampus and delayed hyperactivity-like behavior.

(NE) Cinel C, Boldini A, Russo R, Fox E. Effects of mobile phone electromagnetic fields on an auditory order threshold task. Bioelectromagnetics. 28(6):493-496, 2007. (HU, BE)

The effect of acute exposure to radio frequency electromagnetic fields (RF EMF) generated by mobile phones on an auditory threshold task was investigated. 168 participants performed the task while exposed to RF EMF in one testing session (either global system for mobile communication (GSM) or unmodulated signals) while in a separate session participants were exposed to sham signals. Lateralization effects were tested by exposing participants either on the left side or on the right side of the head. No significant effect of exposure to RF EMF was detected, suggesting that acute exposure to RF EMFs does not affect performance in the order threshold task.

(NE) Cinel C, Russo R, Boldini A, Fox E. Exposure to mobile phone electromagnetic fields and subjective symptoms: a double-blind study. Psychosom Med. 70(3):345-348, 2008. (HU, BE)

OBJECTIVES: The objective of this study was to examine whether acute exposure to radio frequency electromagnetic fields (REFs) emitted by mobile phone may affect subjective symptoms. METHODS: Three large groups of volunteers (total 496) were exposed to REFs emitted by mobile phones in one session and sham signals in a different session. REF and sham exposure sessions were counterbalanced and double blinded. Participants were exposed to either Global System for Mobile Communication (GSM) or unmodulated signals, and the mobile phone was positioned either on the left or on the right side of the head. Before and after REF and sham exposure participants completed a questionnaire to rate five symptoms. Any changes in the severity of the symptoms after REF exposure were compared with changes after sham exposure. RESULTS: For one group of participants (N = 160), it was found that dizziness was affected by GSM exposure, but this was not consistently found with the other two groups of participants. No other significant effects were found. CONCLUSIONS: We did not find consistent evidence suggesting that exposure to mobile phone REFs affect subjective symptoms. Even though we acknowledge that more research is needed, we believe that our results give an important contribution to the research on mobile phone use and subjective symptoms.

(NE) Court-Kowalski S, Finnie JW, Manavis J, Blumbergs PC, Helps SC, Vink R. Effect of long-term (2 years) exposure of mouse brains to global system for mobile communication (GSM) radiofrequency fields on astrocytic immunoreactivity. Bioelectromagnetics. 2015 Feb 20. doi: 10.1002/bem.21891. [Epub ahead of print] (AS, CE, CC)

This study was designed to determine whether long-term (2 years) brain exposure to mobile telephone radiofrequency (RF) fields produces any astrocytic activation as these glia react to a wide range of neural perturbations by astrogliosis. Using a purpose-designed exposure system at 900 MHz, mice were given a single, far-field whole body exposure at a specific absorption rate of 4 W/kg on five successive days per week for 104 weeks. Control mice were sham-exposed or freely mobile in a cage to control any stress caused by immobilization in the exposure module. Brains were perfusion-fixed with 4% paraformaldehyde and three coronal levels immunostained for glial fibrillary acidic protein (GFAP). These brain slices were then examined by light microscopy and the amount of this immunomarker quantified using a color deconvolution method. There was no change in astrocytic GFAP immunostaining in brains after long-term exposure to mobile telephony microwaves compared to control (sham-exposed or freely moving caged mice). It was concluded that long-term (2 years) exposure of murine brains to mobile telephone RF fields did not produce any astrocytic reaction (astrogliosis) detectable by GFAP immunostaining.

(E) Croft RJ, Hamblin DL, Spong J, Wood AW, McKenzie RJ, Stough C. The effect of mobile phone electromagnetic fields on the alpha rhythm of human electroencephalogram. Bioelectromagnetics. 29(1):1-10, 2008. (HU, EE)

Mobile phones (MP) emit low-level electromagnetic fields that have been reported to affect neural function in humans; however, demonstrations of such effects have not been conclusive. The purpose of the present study was to test one of the strongest findings in the literature; that of increased "alpha" power in response to MP-type radiation. Healthy participants (N = 120) were tested using a double-blind counterbalanced crossover design, with each receiving a 30-min Active and a 30-min Sham Exposure 1 week apart, while electroencephalogram (EEG) data were recorded. Resting alpha power (8-12 Hz) was then derived as a function of time, for periods both during and following exposure. Non-parametric analyses were employed as data could not be normalized. Previous reports of an overall alpha power enhancement during the MP exposure were confirmed (relative to Sham), with this effect larger at ipsilateral than contralateral sites over posterior regions. No overall change to alpha power was observed following exposure cessation; however, there was less alpha power contralateral to the exposure source during this period (relative to ipsilateral). Employing a strong methodology, the current findings support previous research that has reported an effect of MP exposure on EEG alpha power.

(E) Croft RJ, Leung S, McKenzie RJ, Loughran SP, Iskra S, Hamblin DL, Cooper NR. Effects of 2G and 3G mobile phones on human alpha rhythms: Resting EEG in adolescents, young adults, and the elderly. Bioelectromagnetics. 31(6):434-444, 2010. (HU, EE, AD, WS)

The present study was conducted to determine whether adolescents and/or the elderly are more sensitive to mobile phone (MP)-related bioeffects than young adults, and to determine this for both 2nd generation (2G) GSM, and 3rd generation (3G) W-CDMA exposures. To test this, resting alpha activity (8-12 Hz band of the electroencephalogram) was assessed because numerous studies have now reported it to be enhanced by MP exposure. Forty-one 13-15 year olds, forty-two 19-40 year olds, and twenty 55-70 year olds were tested using a double-blind

crossover design, where each participant received Sham, 2G and 3G exposures, separated by at least 4 days. Alpha activity, during exposure relative to baseline, was recorded and compared between conditions. Consistent with previous research, the young adults' alpha was greater in the 2G compared to Sham condition, however, no effect was seen in the adolescent or the elderly groups, and no effect of 3G exposures was found in any group. The results provide further support for an effect of 2G exposures on resting alpha activity in young adults, but fail to support a similar enhancement in adolescents or the elderly, or in any age group as a function of 3G exposure.

(NE) Curcio G, Valentini E, Moroni F, Ferrara M, De Gennaro L, Bertini M. Psychomotor performance is not influenced by brief repeated exposures to mobile phones. Bioelectromagnetics. 29(3):237-241, 2008. (HU, BE)

The present study investigated the presence of a cumulative effect of brief and repeated exposures to a GSM mobile phone (902.40 MHz, 217 Hz modulated; peak power of 2 W; average power of 0.25 W; SAR = 0.5 W/kg) on psychomotor functions. To this end, after each of 3 15-min exposures, both an acoustic simple reaction time task (SRTT) and a sequential finger tapping task (SFTT) were administered to 24 subjects. The present study was unable to detect the cumulative effects of brief and repeated EMF exposure on human psychomotor performance, although there was a non-statistical trend to shorter reaction times. In summary, these data show an absence of effects with these particular exposure conditions; however, possible cognitive effects induced by different signal characteristics cannot be excluded.

(E) Curcio G, Ferrara M, Limongi T, Tempesta D, Di Sante G, De Gennaro L, Quaresima V, Ferrari M. Acute mobile phones exposure affects frontal cortex hemodynamics as evidenced by functional near-infrared spectroscopy. J Cereb Blood Flow Metab. 29(5):903-910, 2009. (HU, PE)

This study aimed to evaluate by functional near-infrared spectroscopy (fNIRS), the effects induced by an acute exposure (40 mins) to a GSM (Global System for Mobile Communications) signal emitted by a mobile phone (MP) on the oxygenation of the frontal cortex. Eleven healthy volunteers underwent two sessions (Real and Sham exposure) after a crossover, randomized, double-blind paradigm. The whole procedure lasted 60 mins: 10-mins baseline (Bsl), 40-mins (Exposure), and 10-mins recovery (Post-Exp). Together with frontal hemodynamics, heart rate, objective and subjective vigilance, and self-evaluation of subjective symptoms were also assessed. The fNIRS results showed a slight influence of the GSM signal on frontal cortex, with a linear increase in [HHb] as a function of time in the Real exposure condition ($F(4,40)=2.67$; $P=0.04$). No other measure showed any GSM exposure-dependent changes. These results suggest that fNIRS is a convenient tool for safely and noninvasively investigating the cortical activation in MP exposure experimental settings. Given the short-term effects observed in this study, the results should be confirmed on a larger sample size and using a multichannel instrument that allows the investigation of a wider portion of the frontal cortex.

(NE) Curcio G, Nardo D, Perrucci MG, Pasqualetti P, Chen TL, Del Gratta C, Romani GL, Rossini PM. Effects of mobile phone signals over BOLD response while performing a cognitive task. Clin Neurophysiol. 123(1):129-136, 2012. (HU, BE, PE)

OBJECTIVE: The aim of this study was to investigate the effects induced by an exposure to a GSM signal (Global System for Mobile Communication) on brain BOLD (blood-oxygen-level dependent) response, as well as its time course while performing a Go-NoGo task. **METHODS:** Participants were tested twice, once in presence of a "real" exposure to GSM radiofrequency signal and once under a "sham" exposure (placebo condition). BOLD response of active brain areas and reaction times (RTs) while performing the task were measured both before and after the exposure. **RESULTS:** RTs to the somatosensory task did not change as a function of exposure (real vs sham) to GSM signal. BOLD results revealed significant activations in inferior parietal lobule, insula, precentral and postcentral gyri associated with Go responses after both ''real'' and ''sham'' exposure, whereas no significant effects were observed in the ROI analysis. **CONCLUSIONS:** The present fMRI study did not detect any brain activity changes by mobile phones. Also RTs in a somatosensory task resulted unaffected. **SIGNIFICANCE:** No changes in BOLD response have been observed as a consequence of RF-EMFs exposure.

(NE) Curcio G, Mazzucchi E, Marca GD, Vollono C, Rossini PM. Electromagnetic fields and EEG spiking rate in patients with focal epilepsy. Clin Neurophysiol. 2014 Aug 11. pii: S1388-2457(14)00404-0. doi: 10.1016/j.clinph.2014.07.013. [Epub ahead of print] (HU, EE)

OBJECTIVE: Despite the increase in mobile telephone technology use and possible effects on brain excitability, no studies have investigated the impact of GSM like (Global System for Mobile Communications) signal on the ongoing spiking activity in human epileptic patients. METHODS: Brain electrical (electroencephalogram, EEG) activity of 12 patients with focal epilepsy has been recorded under both Real and Sham exposure following a double-blind, crossover, counterbalanced design: before the exposure (pre-exposure/baseline session), during the Real or Sham 45min exposure (during-exposure session), and after the exposure (post-exposure session). As dependent variables both spiking activity (spikes count) and EEG quantitative indices (spectral power and coherence data) have been considered. RESULTS: Spiking activity tended to be lower under Real than under Sham exposure. EEG spectral content analysis indicated a significant increase of Gamma band under Real exposure, mainly evident in Parieto-occipital and Temporal areas. Connectivity data indicated increased interhemispheric (left temporal to right frontal Regions of Interest, ROIs) instantaneous coherence, in the Beta frequency band during-exposure with respect to baseline session. No significant modification of lagged coherence was observed. CONCLUSIONS: Acute GSM exposure in epileptic patients slightly influences their EEG properties, without reaching any clinical relevance. SIGNIFICANCE: No signs were found of an increased risk of incoming seizures for these patients as a consequence of using mobile phones.

(E) Daniels WM, Pitout IL, Afullo TJ, Mabandla MV. The effect of electromagnetic radiation in the mobile phone range on the behaviour of the rat. Metab Brain Dis. 24(4):629-641, 2009. (AS, ME, BE)

Electromagnetic radiation (EMR) is emitted from electromagnetic fields that surround power lines, household appliances and mobile phones. Research has shown that there are connections between EMR exposure and cancer and also that exposure to EMR may result in structural damage to neurons. In a study by Salford et al. (Environ Health Perspect 111:881-883, 2003) the authors demonstrated the presence of strongly stained areas in the brains of rats that were exposed to mobile phone EMR. These darker neurons were particularly prevalent in the hippocampal area of the brain. The aim of our study was to further investigate the effects of EMR. Since the hippocampus is involved in learning and memory and emotional states, we hypothesised that EMR will have a negative impact on the subject's mood and ability to learn. We subsequently performed behavioural, histological and biochemical tests on exposed and unexposed male and female rats to determine the effects of EMR on learning and memory, emotional states and corticosterone levels. We found no significant differences in the spatial memory test, and morphological assessment of the brain also yielded non-significant differences between the groups. However, in some exposed animals there were decreased locomotor activity, increased grooming and a tendency of increased basal corticosterone levels. These findings suggested that EMR exposure may lead to abnormal brain functioning.

***(NE)** **Danker-Hopfe H, Dorn H, Bornkessel C, Sauter C. Do mobile phone base stations affect sleep of residents? Results from an experimental double-blind sham-controlled field study. Am J Hum Biol. 22(5):613-618, 2010.** **(HU, BE, LI, SL) (*Effects observed probably not caused by exposure to RFR.)**

OBJECTIVES: The aim of the present double-blind, sham-controlled, balanced randomized cross-over study was to disentangle effects of electromagnetic fields (EMF) and non-EMF effects of mobile phone base stations on objective and subjective sleep quality. METHODS: In total 397 residents aged 18-81 years (50.9% female) from 10 German sites, where no mobile phone service was available, were exposed to sham and GSM (Global System for Mobile Communications, 900 MHz and 1,800 MHz) base station signals by an experimental base station while their sleep was monitored at their homes during 12 nights. Participants were randomly exposed to real (GSM) or sham exposure for five nights each. Individual measurement of EMF exposure, questionnaires on sleep disorders, overall sleep quality, attitude towards mobile communication, and on subjective sleep quality (morning and evening protocols) as well as objective sleep data (frontal EEG and EOG recordings) were gathered. RESULTS: Analysis of the subjective and objective sleep data did not reveal any significant differences between the real and sham condition. During sham exposure nights, objective and subjective sleep efficiency, wake after sleep onset, and subjective sleep latency were significantly worse in participants with concerns about possible health risks resulting from base stations than in participants who were not concerned. CONCLUSIONS: The study did not provide any evidence for short-term physiological effects of EMF emitted by mobile phone base stations on objective and subjective sleep quality. However, the results indicate that mobile phone base stations as such (not the electromagnetic fields) may have a significant negative impact on sleep quality.

(NE) Danker-Hopfe H, Dorn H, Bahr A, Anderer P, Sauter C. Effects of electromagnetic fields emitted by mobile phones (GSM 900 and WCDMA/UMTS) on the macrostructure of sleep. J Sleep Res. 20(1 Pt 1):73-81, 2011. (HU, BE, SL)

In the present double-blind, randomized, sham-controlled cross-over study, possible effects of electromagnetic fields emitted by Global System for Mobile Communications (GSM) 900 and Wideband Code-Division Multiple Access (WCDMA)/Universal Mobile Telecommunications System (UMTS) cell-phones on the macrostructure of sleep were investigated in a laboratory environment. An adaptation night, which served as screening night for sleep disorders and as an adjustment night to the laboratory environment, was followed by 9 study nights (separated by a 2-week interval) in which subjects were exposed to three exposure conditions (sham, GSM 900 and WCDMA/UMTS). The sample comprised 30 healthy male subjects within the age range 18-30 years (mean ± standard deviation: 25.3 ± 2.6 years). A cell-phone usage at maximum radio frequency (RF) output power was simulated and the transmitted power was adjusted in order to approach, but not to exceed, the specific absorption rate (SAR) limits of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) guidelines for general public exposure (SAR(10g) = 2.0 W kg(-1)). In this study, possible effects of long-term (8 h) continuous RF exposure on the central nervous system were analysed during sleep, because sleep is a state in which many confounding intrinsic and extrinsic factors (e.g. motivation, personality, attitude) are eliminated or controlled. Thirteen of 177 variables characterizing the initiation and maintenance of sleep in the GSM 900 and three in the WCDMA exposure condition differed from the sham condition. The few significant results are not indicative of a negative impact on sleep architecture. From the present results there is no evidence for a sleep-disturbing effect of GSM 900 and WCDMA exposure.

(E) Danker-Hopfe H, Dorn H, Bolz T, Peter A, Hansen ML, Eggert T, Sauter C. Effects of mobile phone exposure (GSM 900 and WCDMA/UMTS) on polysomnography based sleep quality: An intra- and inter-individual perspective. Environ Res. 145:50-60, 2015. (HU, SL)

BACKGROUND: Studies on effects of radio frequency-electromagnetic fields (RF-EMF) on the macrostructure of sleep so far yielded inconsistent results. This study investigated whether possible effects of RF-EMF exposure differ between individuals. OBJECTIVE: In a double-blind, randomized, sham-controlled cross-over study possible effects of electromagnetic fields emitted by pulsed Global System for Mobile Communications (GSM) 900 and Wideband Code-Division Multiple Access (WCDMA)/Universal Mobile Telecommunications System (WCDMA/UMTS) devices on sleep were analysed. METHODS: Thirty healthy young men (range 18-30 years) were exposed three times per exposure condition while their sleep was recorded. Sleep was evaluated according to the American Academy of Sleep Medicine standard and eight basic sleep variables were considered. RESULTS: Data analyses at the individual level indicate that RF-EMF effects are observed in 90% of the individuals and that all sleep variables are affected in at least four subjects. While sleep of participants was affected in various numbers, combinations of sleep variables and in different directions, showing improvements but also

deteriorations, the only consistent finding was an increase of stage R sleep under GSM 900MHz exposure (9 of 30 subjects) as well as under WCDMA/UMTS exposure (10 of 30 subjects). CONCLUSIONS: The results underline that sleep of individuals can be affected differently. The observations found here may indicate an underlying thermal mechanism of RF-EMF on human REM sleep. Nevertheless, the effect of an increase in stage R sleep in one third of the individuals does not necessarily indicate a disturbance of sleep.

(E) Dasdag S, Akdag MZ, Ulukaya E, Uzunlar AK, Ocak AR. Effect of mobile phone exposure on apoptotic glial cells and status of oxidative stress in rat brain. Electromagn Biol Med. 28(4):342-354, 2009. (AS, CE, CC, OX)

The aim of this study was to investigate the effects of mobile phone exposure on glial cells in brain. The study carried out on 31 Wistar Albino adult male rats. The rat heads in a carousel exposed to 900 MHz microwave. For the study group (n:14), rats exposed to the radiation 2 h per day (7 days in a week) for 10 months. For the sham group (n:7), rats were placed into the carousel and the same procedure was applied except that the generator was turned off. For the cage control (n:10), nothing applied to rats in this group. In this study, rats were euthanized after 10 months of exposure periods and brains were removed. Brain tissues were immunohistochemically stained for the active (cleaved) caspase-3, which is a well-known apoptosis marker, and p53. The expression of the proteins was evaluated by a semi-quantitative scoring system. However, total antioxidative capacity (TAC), catalase, total oxidant status (TOS), and oxidative stress index were measured in rat brain. Final score for apoptosis in the exposed group was significantly lower than the sham ($p < 0.001$) and the cage control groups ($p < 0.01$). p53 was not significantly changed by the exposure ($p > 0.05$). The total antioxidant capacity and catalase in the experimental group was found higher than that in the sham group ($p < 0.001$, $p < 0.05$). In terms of the TOS and oxidative stress index, there was no statistically significant difference between exposure and sham groups ($p > 0.05$). In conclusion, the final score for apoptosis, total antioxidant capacity and catalase in rat brain might be altered by 900 MHz radiation produced by a generator to represent exposure of global systems for mobile communication (GSM) cellular phones.

(E) Dasdag S, Akdag MZ, Kizil G, Kizil M, Cakir DU, Yokus B. Effect of 900 MHz radio frequency radiation on beta amyloid protein, protein carbonyl, and malondialdehyde in the brain. Electromagn Biol Med. 31(1):67-74, 2012. (AS, CE, CH, OX)

Recently, many studies have been carried out in relation to 900 MHz radiofrequency radiation (RF) emitted from a mobile phone on the brain. However, there is little data concerning possible mechanisms between long-term exposure of RF radiation and biomolecules in brain. Therefore, we aimed to investigate long-term effects of 900 MHz radiofrequency radiation on beta amyloid protein, protein carbonyl, and malondialdehyde in the rat brain. The study was carried out on 17 Wistar Albino adult male rats. The rat heads in a carousel were exposed to 900 MHz radiofrequency radiation emitted from a generator, simulating mobile phones. For the study group (n: 10), rats were exposed to the radiation 2 h per day (7 days a week) for 10

months. For the sham group (n: 7), rats were placed into the carousel and the same procedure was applied except that the generator was turned off. In this study, rats were euthanized after 10 months of exposure and their brains were removed. Beta amyloid protein, protein carbonyl, and malondialdehyde levels were found to be higher in the brain of rats exposed to 900 MHz radiofrequency radiation. However, only the increase of protein carbonyl in the brain of rats exposed to 900 MHz radiofrequency radiation was found to be statistically significant ($p<0.001$). In conclusion, 900 MHz radiation emitted from mobile/cellular phones can be an agent to alter some biomolecules such as protein. However, further studies are necessary.

(E) Dasdag S, Akdag MZ, Erdal ME, Erdal N, Ay OI, Ay ME, Yilmaz SG, Tasdelen B, Yegin K. Long term and excessive use of 900 MHz radiofrequency radiation alter microRNA expression in brain. Int J Radiat Biol. 2014 Dec 20:1-22. [Epub ahead of print]. (AS, CE, CH)

Purpose: We still do not have any information on the interaction between radiofrequency radiation (RF) and miRNAs, which play paramount role in growth, differentiation, proliferation and cell death by suppressing one or more target genes. The purpose of this study is to bridge this gap by investigating effects of long term 900 MHz mobile phone exposure on some of the miRNAs in brain tissue. Materials and Methods: The study was carried out on fourteen Wistar Albino adult male rats by dividing them into two groups: sham (n: 7) and exposure (n: 7). Rats in the exposure group were exposed to 900 MHz RF radiation for 3 h per day (7 d a week) for twelve months (one year). The same procedure was applied to the rats in the sham group except the generator was turned off. Immediately after the last exposure, rats were sacrificed and their brains were removed. rno-miR-9-5p, rno-miR-29a-3p, rno-miR-106b-5p, rno-miR-107 and rno-miR-125a-3p in brain were investigated in detail. Results: Results revealed that long term exposure of 900 MHz RF radiation only decreased rno-miR107 (adjP*= 0,045) value where the whole body (rms) SAR value was 0.0369 W/kg. However, our results indicated that other micro RNAs evaluated in this study was not altered by 900 MHz RF radiation. Conclusion: 900 MHz RF radiation can alter some of the miRNAs, which, in turn, may lead to adverse effects. Therefore, further studies should be performed.

(NE) de Gannes FP, Billaudel B, Taxile M, Haro E, Ruffié G, Lévêque P, Veyret B, Lagroye I. Effects of head-only exposure of rats to GSM-900 on blood-brain barrier permeability and neuronal degeneration. Radiat Res. 172(3):359-367, 2009. (AS, CE, ME, CC)

Salford et al. reported in 2003 that a single 2-h exposure to GSM-900 mobile telephony signals induced brain damage (increased permeability of the blood-brain barrier and presence of dark neurons) 50 days after exposure. In our study, 16 Fischer 344 rats (14 weeks old) were exposed head-only to the GSM-900 signal for 2 h at various brain-averaged SARs (0, 0.14 and 2.0 W/kg) or were used as cage or positive controls. Albumin leakage and neuron degeneration were evaluated 14 and 50 days after exposure. No apoptotic neurons were found 14 days after the last exposure using the TUNEL method. No statistically significant albumin leakage was

observed. Neuronal degeneration, assessed using cresyl violet or the more specific marker Fluoro-Jade B, was not significantly different among the tested groups. No apoptotic neurons were detected. The findings of our study did not confirm the previous results of Salford et al.

(E) de Tommaso M, Rossi P, Falsaperla R, Francesco Vde V, Santoro R, Federici A. Mobile phones exposure induces changes of contingent negative variation in humans. Neurosci Lett. 464(2):79-83, 2009. (HU, EE)

Event-related potentials have been largely employed to test effects of GSM emissions on human brain. The aim of the present study was the evaluation of initial contingent negative variation (iCNV) changes, induced by 900 MHz GSM exposure, in a double blind design in healthy volunteers, subjected to a threefold experimental condition, EXPOSED (A), a real GSM phone emitting electromagnetic power, SHAM (B), a real phone where the electromagnetic power was dissipated on an internal load and OFF (C), a phone completely switched-off. Ten healthy right-handed volunteers were evaluated. The CNV was recorded during a 10 min time interval in each of the three experimental conditions A, B, and C, in order to assess the iCNV amplitude and habituation. The iCNV amplitude decreased and habituation increased during both A and B conditions, compared with condition C. This effect was diffuse over the scalp, and there was no significant prevalence of iCNV amplitude reduction on the left side, were the phones were located. Mobile Phones exposures A and B seemed to act on brain electrical activity, reducing the arousal and expectation of warning stimulus. This evidence, limited by the low number of subjects investigated, could be explained in terms of an effect induced by both the GSM signal and the extremely low frequency magnetic field produced by battery and internal circuits.

(E) Del Vecchio G, Giuliani A, Fernandez M, Mesirca P, Bersani F, Pinto R, Ardoino L, Lovisolo GA, Giardino L, Calzà L. Effect of radiofrequency electromagnetic field exposure on in vitro models of neurodegenerative disease. Bioelectromagnetics. 30(7):564-572, 2009. (CS, CE, IA, OX)

In this work we tested viability, proliferation, and vulnerability of neural cells, after continuous radiofrequency (RF) electromagnetic fields exposure (global system for mobile telecommunications (GSM) modulated 900 MHz signal at a specific absorption rate (SAR) of 1 W/kg and maximum duration 144 h) generated by transverse electromagnetic cells. We used two cellular systems, SN56 cholinergic for example, SN56 cholinergic cell line and rat primary cortical neurons, and well-known neurotoxic challenges, such as glutamate, 25-35AA beta-amyloid, and hydrogen peroxide. Exposure to RF did not change viability/proliferation rate of the SN56 cholinergic cells or viability of cortical neurons. Co-exposure to RF exacerbated neurotoxic effect of hydrogen peroxide in SN56, but not in primary cortical neurons, whereas no cooperative effects of RF with glutamate and 25-35AA beta-amyloid were found. These data suggest that only under particular circumstances exposure to GSM modulated, 900 MHz signal act as a co-stressor for oxidative damage of neural cells.

(E) Del Vecchio G, Giuliani A, Fernandez M, Mesirca P, Bersani F, Pinto R, Ardoino L, Lovisolo GA, Giardino L, Calzà L. Continuous exposure to 900MHz GSM-modulated EMF alters morphological maturation of neural cells. Neurosci Lett. 455(3):173-177, 2009. (CS, ME, DE)

The effects of radiofrequency electromagnetic field (RF-EMF) exposure on neuronal phenotype maturation have been studied in two different in vitro models: murine SN56 cholinergic cell line and rat primary cortical neurons. The samples were exposed at a dose of 1W/kg at 900 MHz GSM modulated. The phenotype analysis was carried out at 48 and 72 h (24 and 48 h of SN56 cell line differentiation) or at 24, 72, 120 h (2, 4 and 6 days in vitro for cortical neurons) of exposure, on live and immunolabeled neurons, and included the morphological study of neurite emission, outgrowth and branching. Moreover, cortical neurons were studied to detect alterations in the expression pattern of cytoskeleton regulating factors, e.g. beta-thymosin, and of early genes, e.g. c-Fos and c-Jun through real-time PCR on mRNA extracted after 24h exposure to EMF. We found that RF-EMF exposure reduced the number of neurites generated by both cell systems, and this alteration correlates to increased expression of beta-thymosin mRNA.

(E) Deniz OG, Kaplan S, Selcuk MB, Terzi M, Altun, Yurt KK, Aslan K, Davis D. Effects of short and long term electromagnetic fields exposure on the human hippocampus. J Micros Ultrastru (2017, In press) (HU, ME, BE)

The increasing use of mobile phones may have a number of physiological and psychological effects on human health. Many animal and human studies have reported various effects on the central nervous system and cognitive performance from of exposure to electromagnetic fields (EMF) emitted by mobile phones. The aim of the present study was to evaluate the effects of mobile phones on the morphology of the human brain and on cognitive performance using stereological and spectroscopic methods and neurocognitive tests. Sixty healthy female medical school students aged 18–25 years were divided into a low exposure group (30 subjects, <30 min daily use by the head) and high exposure group (30 subjects, >90 min daily use by the head). Magnetic resonance images (MRI) of the brain analysed on OsiriX 3.2.1 workstation. Neuropsychological tests were performed for each subject. In addition, three dominant specific metabolites were analysed, choline at 3.21 ppm, creatine at 3.04 ppm and N-acetyl aspartate at 2.02 ppm. Analysis of the spectroscopic results revealed no significant difference in specific metabolites between the groups ($p > 0.05$). There was also no significant difference in terms of hippocampal volume between the groups ($p > 0.05$). In contrast, the results of the stroop and digit span (backward) neurocognitive tests of high exposure group for evaluating attention were significantly poorer from low exposure group ($p < 0.05$). Based on these results, we conclude that a lack of attention and concentration may occur in subjects who talk on mobile phones for longer times, compared to those who use phones relatively less.

(E) Deshmukh PS, Banerjee BD, Abegaonkar MP, Megha K, Ahmed RS, Tripathi AK, Mediratta PK. Effect of low level microwave radiation exposure on cognitive function and oxidative stress in rats. Indian J Biochem Biophys. 50(2):114-119, 2013a. (AS, LI, CE, BE, OX)

Use of wireless communicating devices is increasing at an exponential rate in present time and is raising serious concerns about possible adverse effects of microwave (MW) radiation emitted from these devices on human health. The present study aimed to evaluate the effects of 900 MHz MW radiation exposure on cognitive function and oxidative stress in blood of Fischer rats. Animals were divided into two groups (6 animals/group): Group I (MW-exposed) and Group II (Sham-exposed). Animals were subjected to MW exposure (Frequency 900 MHz; specific absorption rate 8.4738 x 10(-5) W/kg) in Gigahertz transverse electromagnetic cell (GTEM) for 30 days (2 h/day, 5 days/week). Subsequently, cognitive function and oxidative stress parameters were examined for each group. Results showed significant impairment in cognitive function and increase in oxidative stress, as evidenced by the increase in levels of MDA (a marker of lipid peroxidation) and protein carbonyl (a marker of protein oxidation) and unaltered GSH content in blood. Thus, the study demonstrated that low level MW radiation had significant effect on cognitive function and was also capable of leading to oxidative stress.

(E) Deshmukh PS, Megha K, Banerjee BD, Ahmed RS, Chandna S, Abegaonkar MP, Tripathi AK. Detection of Low Level Microwave Radiation Induced Deoxyribonucleic Acid Damage Vis-à-vis Genotoxicity in Brain of Fischer Rats. Toxicol Int. 20(1):19-24, 2013b. (AS, LI, CE, CH)

BACKGROUND: Non-ionizing radiofrequency radiation has been increasingly used in industry, commerce, medicine and especially in mobile phone technology and has become a matter of serious concern in present time. OBJECTIVE: The present study was designed to investigate the possible deoxyribonucleic acid (DNA) damaging effects of low-level microwave radiation in brain of Fischer rats. MATERIALS AND METHODS: Experiments were performed on male Fischer rats exposed to microwave radiation for 30 days at three different frequencies: 900, 1800 and **2450 MHz**. Animals were divided into 4 groups: Group I (Sham exposed): Animals not exposed to microwave radiation but kept under same conditions as that of other groups, Group II: Animals exposed to microwave radiation at frequency 900 **MHz** at specific absorption rate (SAR) 5.953 × 10(-4) W/kg, Group III: Animals exposed to 1800 **MHz** at SAR 5.835 × 10(-4) W/kg and Group IV: Animals exposed to **2450 MHz** at SAR 6.672 × 10(-4) W/kg. At the end of the exposure period animals were sacrificed immediately and DNA damage in brain tissue was assessed using alkaline comet assay. RESULTS: In the present study, we demonstrated DNA damaging effects of low level microwave radiation in brain. CONCLUSION: We concluded that low SAR microwave radiation exposure at these frequencies may induce DNA strand breaks in brain tissue.

(E) Deshmukh PS, Nasare N, Megha K, Banerjee BD, Ahmed RS, Singh D, Abegaonkar MP, Tripathi AK, Mediratta PK. Cognitive Impairment and Neurogenotoxic Effects in Rats Exposed to Low-Intensity Microwave Radiation. Int J Toxicol. 2015 Mar 5. pii: 1091581815574348. [Epub ahead of print] (AS, CE, LI, BE, CH)

The health hazard of microwave radiation (MWR) has become a recent subject of interest as a result of the enormous increase in mobile phone usage. The present study aimed to investigate the effects of chronic low-intensity microwave exposure on cognitive function, heat shock

protein 70 (HSP70), and DNA damage in rat brain. Experiments were performed on male Fischer rats exposed to MWR for 180 days at 3 different frequencies, namely, 900, 1800 MHz, and 2450 MHz. Animals were divided into 4 groups: group I: sham exposed; group II: exposed to MWR at 900 MHz, specific absorption rate (SAR) 5.953×10^{-4} W/kg; group III: exposed to 1800 MHz, SAR 5.835×10^{-4} W/kg; and group IV: exposed to 2450 MHz, SAR 6.672×10^{-4} W/kg. All the rats were tested for cognitive function at the end of the exposure period and were subsequently sacrificed to collect brain. Level of HSP70 was estimated by enzyme-linked immunotarget assay and DNA damage was assessed using alkaline comet assay in all the groups. The results showed declined cognitive function, elevated HSP70 level, and DNA damage in the brain of microwave-exposed animals. The results indicated that, chronic low-intensity microwave exposure in the frequency range of 900 to 2450 MHz may cause hazardous effects on the brain.

(E) Deshmukh PS, Megha K, Nasare N, Banerjee BD, Ahmed RS, Abegaonkar MP, Tripathi AK, Mediratta PK. Effect of Low Level Subchronic Microwave Radiation on Rat Brain. Biomed Environ Sci. 29(12):858-867, 2016. (AS, LI, CE, BE, CC)

OBJECTIVE: The present study was designed to investigate the effects of subchronic low level microwave radiation (MWR) on cognitive function, heat shock protein 70 (HSP70) level and DNA damage in brain of Fischer rats. METHODS: Experiments were performed on male Fischer rats exposed to microwave radiation for 90 days at three different frequencies: 900, 1800, and 2450 MHz. Animals were divided into 4 groups: Group I: Sham exposed, Group II: animals exposed to microwave radiation at 900 MHz and specific absorption rate (SAR) 5.953 × 10-4 W/kg, Group III: animals exposed to 1800 MHz at SAR 5.835 × 10-4 W/kg and Group IV: animals exposed to 2450 MHz at SAR 6.672 × 10-4 W/kg. All the animals were tested for cognitive function using elevated plus maze and Morris water maze at the end of the exposure period and subsequently sacrificed to collect brain tissues. HSP70 levels were estimated by ELISA and DNA damage was assessed using alkaline comet assay. RESULTS: Microwave exposure at 900-2450 MHz with SAR values as mentioned above lead to decline in cognitive function, increase in HSP70 level and DNA damage in brain. CONCLUSION: The results of the present study suggest that low level microwave exposure at frequencies 900, 1800, and 2450 MHz may lead to hazardous effects on brain.

(E) Divan HA, Kheifets L, Obel C, Olsen J. Prenatal and postnatal exposure to cell phone use and behavioral problems in children. Epidemiology. 19(4):523-529, 2008. (HU, DE, BE)

BACKGROUND: The World Health Organization has emphasized the need for research into the possible effects of radiofrequency fields in children. We examined the association between prenatal and postnatal exposure to cell phones and behavioral problems in young children. METHODS: Mothers were recruited to the Danish National Birth Cohort early in pregnancy. When the children of those pregnancies reached 7 years of age in 2005 and 2006, mothers were asked to complete a questionnaire regarding the current health and behavioral status of children, as well as past exposure to cell phone use. Mothers evaluated the child's behavior problems using the Strength and Difficulties Questionnaire. RESULTS: Mothers of 13,159

children completed the follow-up questionnaire reporting their use of cell phones during pregnancy as well as current cell phone use by the child. Greater odds ratios for behavioral problems were observed for children who had possible prenatal or postnatal exposure to cell phone use. After adjustment for potential confounders, the odds ratio for a higher overall behavioral problems score was 1.80 (95% confidence interval = 1.45-2.23) in children with both prenatal and postnatal exposure to cell phones. CONCLUSIONS: Exposure to cell phones prenatally-and, to a lesser degree, postnatally-was associated with behavioral difficulties such as emotional and hyperactivity problems around the age of school entry. These associations may be noncausal and may be due to unmeasured confounding. If real, they would be of public health concern given the widespread use of this technology.

(NE) Divan HA, Kheifets L, Olsen J. Prenatal cell phone use and developmental milestone delays among infants. Scand J Work Environ Health. 37(4):341-348, 2011. (HU, DE, BE)

OBJECTIVE: The aim of this study was to examine if prenatal use of cell phones by pregnant mothers is associated with developmental milestones delays among offspring up to 18 months of age. **METHODS:** Our work is based upon the Danish National Birth Cohort (DNBC), which recruited pregnant mothers from 1996-2002, and was initiated to collect a variety of detailed information regarding in utero exposures and various health outcomes. At the end of 2008, over 41,000 singleton, live births had been followed with the Age-7 questionnaire, which collected cell phone use exposure for mothers during pregnancy. Outcomes for developmental milestones were obtained from telephone interviews completed by mothers at age 6 and 18 months postpartum. **RESULTS:** A logistic regression model estimated the odds ratios (OR) for developmental milestone delays, adjusted for potential confounders. Less than 5% of children at age 6 and 18 months had cognitive/language or motor developmental delays. At 6 months, the adjusted OR was 0.8 [95% confidence interval (95% CI) 0.7-1.0] for cognitive/language delay and 0.9 (95% CI 0.8-1.1) for motor development delay. At 18 months, the adjusted OR were 1.1 (95% CI 0.9-1.3) and 0.9 (95% CI 0.8-1.0) for cognitive/language and motor development delay, respectively. **CONCLUSIONS:** No evidence of an association between prenatal cell phone use and motor or cognitive/language developmental delays among infants at 6 and 18 months of age was observed. Even when considering dose-response associations for cell phone, associations were null.

(E) Divan HA, Kheifets L, Obel C, Olsen J. Cell phone use and behavioural problems in young children. J Epidemiol Community Health. 66(6):524-529, 2012. (HU, DE, BE)

BACKGROUND: Potential health effects of cell phone use in children have not been adequately examined. As children are using cell phones at earlier ages, research among this group has been identified as the highest priority by both national and international organisations. The authors previously reported results from the Danish National Birth Cohort (DNBC), which looked at prenatal and postnatal exposure to cell phone use and behavioural problems at age 7 years. Exposure to cell phones prenatally, and to a lesser degree postnatally, was associated with more behavioural difficulties. The original analysis included nearly 13 000 children who reached age 7 years by November 2006. **METHODS:** To see if a larger, separate group of DNBC children

would produce similar results after considering additional confounders, children of mothers who might better represent current users of cell phones were analysed. This 'new' dataset consisted of 28 745 children with completed Age-7 Questionnaires to December 2008. **RESULTS:** The highest OR for behavioural problems were for children who had both prenatal and postnatal exposure to cell phones compared with children not exposed during either time period. The adjusted effect estimate was 1.5 (95% CI 1.4 to 1.7). **CONCLUSIONS:** The findings of the previous publication were replicated in this separate group of participants demonstrating that cell phone use was associated with behavioural problems at age 7 years in children, and this association was not limited to early users of the technology. Although weaker in the new dataset, even with further control for an extended set of potential confounders, the associations remained.

(NE) Dogan M, Turtay MG, Oguzturk H, Samdanci E, Turkoz Y, Tasdemir S, Alkan A, Bakir S. Effects of electromagnetic radiation produced by 3G mobile phones on rat brains: magnetic resonance spectroscopy, biochemical, and histopathological evaluation. Hum Exp Toxicol. 31(6):557-564, 2012. (AS, CE, OX, CC, CH)

Objective: The effects of electromagnetic radiation (EMR) produced by a third-generation (3G) mobile phone (MP) on rat brain tissues were investigated in terms of magnetic resonance spectroscopy (MRS), biochemistry, and histopathological evaluations. Methods: The rats were randomly assigned to two groups: Group 1 is composed of 3G-EMR-exposed rats (n = 9) and Group 2 is the control group (n = 9). The first group was subjected to EMR for 20 days. The control group was not exposed to EMR. Choline (Cho), creatinin (Cr), and N-acetylaspartate (NAA) levels were evaluated by MRS. Catalase (CAT) and glutathione peroxidase (GSH-Px) enzyme activities were measured by spectrophotometric method. Histopathological analyses were carried out to evaluate apoptosis in the brain tissues of both groups. Results: In MRS, NAA/Cr, Cho/Cr, and NAA/Cho ratios were not significantly different between Groups 1 and 2. Neither the oxidative stress parameters, CAT and GSH-Px, nor the number of apoptotic cells were significantly different between Groups 1 and 2. Conclusions: Usage of short-term 3G MP does not seem to have a harmful effect on rat brain tissue.

(E) Dragicevic N, Bradshaw PC, Mamcarz M, Lin X, Wang L, Cao C, Arendash GW. Long-term electromagnetic field treatment enhances brain mitochondrial function of both Alzheimer's transgenic mice and normal mice: a mechanism for electromagnetic field-induced cognitive benefit? Neuroscience 185:135-149, 2011. (AS, CE, CC, OX, MA)

We have recently reported that long-term exposure to high frequency electromagnetic field (EMF) treatment not only prevents or reverses cognitive impairment in Alzheimer's transgenic (Tg) mice, but also improves memory in normal mice. To elucidate the possible mechanism(s) for these EMF-induced cognitive benefits, brain mitochondrial function was evaluated in aged Tg mice and non-transgenic (NT) littermates following 1 month of daily EMF exposure. In Tg mice, EMF treatment enhanced brain mitochondrial function by 50-150% across six established measures, being greatest in cognitively-important brain areas (e.g. cerebral cortex and hippocampus). EMF treatment also increased brain mitochondrial function in normal aged

mice, although the enhancement was not as robust and less widespread compared to that of Tg mice. The EMF-induced enhancement of brain mitochondrial function in Tg mice was accompanied by 5-10 fold increases in soluble Aβ1-40 within the same mitochondrial preparations. These increases in mitochondrial soluble amyloid-β peptide (Aβ) were apparently due to the ability of EMF treatment to disaggregate Aβ oligomers, which are believed to be the form of Aβ causative to mitochondrial dysfunction in Alzheimer's disease (AD). Finally, the EMF-induced mitochondrial enhancement in both Tg and normal mice occurred through non-thermal effects because brain temperatures were either stable or decreased during/after EMF treatment. These results collectively suggest that brain mitochondrial enhancement may be a primary mechanism through which EMF treatment provides cognitive benefit to both Tg and NT mice. Especially in the context that mitochondrial dysfunction is an early and prominent characteristic of Alzheimer's pathogenesis, EMF treatment could have profound value in the disease's prevention and treatment through intervention at the mitochondrial level.

(E) Eberhardt JL, Persson BR, Brun AE, Salford LG, Malmgren LO. Blood-brain barrier permeability and nerve cell damage in rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones. Electromagn Biol Med. 27(3):215-229, 2008. (AS, ME, CC, LI)

We investigated the effects of global system for mobile communication (GSM) microwave exposure on the permeability of the blood-brain barrier and signs of neuronal damage in rats using a real GSM programmable mobile phone in the 900 MHz band. Ninety-six non-anaesthetized rats were either exposed to microwaves or sham exposed in TEM-cells for 2 h at specific absorption rates of average whole-body Specific Absorption Rates (SAR) of 0.12, 1.2, 12, or 120 mW/kg. The rats were sacrificed after a recovery time of either 14 or 28 d, following exposure and the extravazation of albumin, its uptake into neurons, and occurrence of damaged neurons was assessed. Albumin extravazation and also its uptake into neurons was seen to be enhanced after 14 d (Kruskal Wallis test: $p = 0.02$ and 0.002, respectively), but not after a 28 d recovery period. The occurrence of dark neurons in the rat brains, on the other hand, was enhanced later, after 28 d ($p = 0.02$). Furthermore, in the 28-d brain samples, neuronal albumin uptake was significantly correlated to occurrence of damaged neurons (Spearman $r = 0.41$; $p < 0.01$).

(NE) Eltiti S, Wallace D, Ridgewell A, Zougkou K, Russo R, Sepulveda F, Fox E. Short-term exposure to mobile phone base station signals does not affect cognitive functioning or physiological measures in individuals who report sensitivity to electromagnetic fields and controls. Bioelectromagnetics. 30(7):556-563, 2009. (HU, BE, LI)

Individuals who report sensitivity to electromagnetic fields often report cognitive impairments that they believe are due to exposure to mobile phone technology. Previous research in this area has revealed mixed results, however, with the majority of research only testing control individuals. Two studies using control and self-reported sensitive participants found inconsistent effects of mobile phone base stations on cognitive functioning. The aim of the present study was to clarify whether short-term (50 min) exposure at 10 mW/m(2) to typical Global System for Mobile Communication (GSM) and Universal Mobile Telecommunications

System (UMTS) base station signals affects attention, memory, and physiological endpoints in sensitive and control participants. Data from 44 sensitive and 44 matched-control participants who performed the digit symbol substitution task (DSST), digit span task (DS), and a mental arithmetic task (MA), while being exposed to GSM, UMTS, and sham signals under double-blind conditions were analyzed. Overall, cognitive functioning was not affected by short-term exposure to either GSM or UMTS signals in the current study. Nor did exposure affect the physiological measurements of blood volume pulse (BVP), heart rate (HR), and skin conductance (SC) that were taken while participants performed the cognitive tasks.

(E) Erdem Koç G, Kaplan S, Altun G, Gümüş H, Gülsüm Deniz Ö, Aydin I, Emin Onger M, Altunkaynak Z. Neuroprotective effects of melatonin and omega-3 on hippocampal cells prenatally exposed to 900 MHz electromagnetic fields. Int J Radiat Biol. 2016 Jul 21:1-6. [Epub ahead of print] (AS, CE, DE, CC, IA)

PURPOSE: Adverse effects on human health caused by electromagnetic fields (EMF) associated with the use of mobile phones, particularly among young people, are increasing all the time. The potential deleterious effects of EMF exposure resulting from mobile phones being used in close proximity to the brain require particular evaluation. However, only a limited number of studies have investigated the effects of prenatal exposure to EMF in the development of the pyramidal cells using melatonin (MEL) and omega-3 (ω-3). MATERIALS AND METHODS: We established seven groups of pregnant rats consisting of three animals each; control (CONT), SHAM, EMF, EMF + MEL, MEL, EMF + ω-3 and ω-3 alone. The rats in the EMF, EMF + MEL, EMF + ω-3 groups were exposed to 900 MHz EMF for 60 min/day in an exposure tube during the gestation period. The CONT, MEL and ω-3 group rats were not placed inside the exposure tube or exposed to EMF during the study period. After delivery, only spontaneously delivered male rat pups were selected for the establishment of further groups. Each group of offspring consisted of six animals. The optical fractionator technique was used to determine total pyramidal neuron numbers in the rat hippocampal region. RESULTS: The total number of pyramidal cells in the cornu ammonis (CA) in the EMF group was significantly lower than in the CONT, SHAM, EMF + MEL, and EMF + ω-3 groups. No significant difference was observed between the EMF, MEL and ω-3 groups. No difference was also observed between any groups in terms of rats' body or brain weights. CONCLUSION: MEL and ω-3 can protect the cell against neuronal damage in the hippocampus induced by 900 MHz EMF. However, further studies are now needed to evaluate the chronic effects of 900 MHz EMF on the brain in the prenatal period.

(E) Eser O, Songur A, Aktas C, Karavelioglu E, Caglar V, Aylak F, Ozguner F, Kanter M. The effect of electromagnetic radiation on the rat brain: an experimental study. Turk Neurosurg. 23(6):707-715, 2013. (AS, CE, OX, ME)

AIM: The aim of this study is to determine the structural changes of electromagnetic waves in the frontal cortex, brain stem and cerebellum. MATERIAL and METHODS: 24 Wistar Albino adult male rats were randomly divided into four groups: group I consisted of control rats, and groups II-IV comprised electromagnetically irradiated (EMR) with 900, 1800 and 2450 MHz. The heads of the rats were exposed to 900, 1800 and 2450 MHz microwaves irradiation for 1h per day for 2 months. RESULTS: While the histopathological changes in the frontal cortex and brain stem

were normal in the control group, there were severe degenerative changes, shrunken cytoplasm and extensively dark pyknotic nuclei in the EMR groups. Biochemical analysis demonstrated that the Total Antioxidative Capacity level was significantly decreased in the EMR groups and also Total Oxidative Capacity and Oxidative Stress Index levels were significantly increased in the frontal cortex, brain stem and cerebellum. IL-1β level was significantly increased in the EMR groups in the brain stem. CONCLUSION: EMR causes to structural changes in the frontal cortex, brain stem and cerebellum and impair the oxidative stress and inflammatory cytokine system. This deterioration can cause to disease including loss of these areas function and cancer development.

(NE) Fasseas MK, Fragopoulou AF, Manta AK, Skouroliakou A, Vekrellis K, Margaritis LH, Syntichaki P. Response of Caenorhabditis elegans to wireless devices radiation exposure. Int J Radiat Biol. 91:286-293, 2015. (AS, CE, BE, OX)

Purpose: The aim of this study was to examine the impact of electromagnetic radiation, produced by GSM (Global System for Mobile communications) mobile phones, Wi-Fi (Wireless-Fidelity) routers and wireless DECT (Digital Enhanced Cordless Telecommunications) phones, on the nematode C. elegans. Materials and methods: We exposed synchronized populations, of different developmental stages, to these wireless devices at E-field levels below ICNIRP's (International Commission on Non-Ionizing Radiation Protection) guidelines for various lengths of time. WT (wild-type) and aging- or stress-sensitive mutant worms were examined for changes in growth, fertility, lifespan, chemotaxis, short-term memory, increased ROS (Reactive Oxygen Species) production and apoptosis by using fluorescent marker genes or qRT-PCR (quantitative Reverse Transcription-Polymerase Chain Reaction). Results: No statistically significant differences were found between the exposed and the sham/control animals in any of the experiments concerning lifespan, fertility, growth, memory, ROS, apoptosis or gene expression. Conclusions: The worm appears to be robust to this form of (pulsed) radiation, at least under the exposure conditions used.

(E) Favre D. Mobile phone-induced honeybee worker piping Apidologie 42:270–279, 2011. (AS, BE)

The worldwide maintenance of the honeybee has major ecological, economic, and political implications. In the present study, electromagnetic waves originating from mobile phones were tested for potential effects on honeybee behavior. Mobile phone handsets were placed in the close vicinity of honeybees. The sound made by the bees was recorded and analyzed. The audiograms and spectrograms revealed that active mobile phone handsets have a dramatic impact on the behavior of the bees, namely by inducing the worker piping signal. In natural conditions, worker piping either announces the swarming process of the bee colony or is a signal of a disturbed bee colony.

(NE) Finnie JW, Blumbergs PC, Cai Z, Manavis J. Expression of the water channel protein, aquaporin-4, in mouse brains exposed to mobile telephone radiofrequency fields. Pathology. 41(5):473-475, 2009a. (AS, CE, CC)

AIM: To determine whether exposure to mobile telephone radiofrequency (RF) fields, either acutely or long-term, produces up-regulation of the water channel protein, aquaporin-4 (AQP-4). **METHODS:** Using a purpose-designed exposure system at 900 MHz, mice were given a single, far-field whole body exposure at a specific absorption rate of 4 W/kg for 60 minutes or a similar exposure on 5 successive days/week for 104 weeks. Control mice were sham-exposed or freely mobile in a cage to control for any stress caused by restraint in the exposure module. A positive control group was given a clostridial toxin known to cause microvascular endothelial injury, severe vasogenic oedema and upregulation of AQP-4. Brains were perfusion fixed with 4% paraformaldehyde, coronal sections cut from six levels, and immunostained for the principal water channel protein in brain, AQP-4. **RESULTS:** There was no increase in AQP-4 expression in brains exposed to mobile phone microwaves compared to control (sham exposed and freely moving caged mice) brains after short or protracted exposure, while AQP-4 was substantially upregulated in the brains of mice given the clostridial toxin. **CONCLUSION:** Brains exposed to mobile telephone RF fields for a short (60 minutes) or long (2 years) duration did not show any immunohistochemically detectable up-regulation of the water channel protein, AQP-4, suggesting that there was no significant increase in blood-brain barrier permeability.

(NE) Finnie JW, Chidlow G, Blumbergs PC, Manavis J, Cai Z. Heat shock protein induction in fetal mouse brain as a measure of stress after whole of gestation exposure to mobile telephony radiofrequency fields. Pathology. 41(3):276-279, 2009b. (AS, LE, CC, DE)

AIM: To determine whether whole of gestation exposure of fetal mouse brain to mobile telephone radiofrequency fields produces a stress response detectable by induction of heat shock proteins (HSPs). **METHODS:** Using a purpose-designed exposure system at 900 MHz, pregnant mice were given a single, far-field, whole body exposure at a specific absorption rate of 4 W/kg for 60 min/day from day 1 to day 19 of gestation. Control mice were sham-exposed or freely mobile in a cage to control for any stress caused by restraint in the exposure module. Immediately prior to parturition on day 19, fetal brains were collected, fixed in 4% paraformaldehyde and paraffin-embedded. Three coronal sections encompassing a wide range of anatomical regions were cut from each brain and any stress response detected by immunostaining for HSP25, 32 and 70. **RESULTS:** There was no induction of HSP32 or 70 in any brains, while HSP25 expression was limited to two brainstem nuclei and occurred consistently in exposed and non-exposed brains. **CONCLUSION:** Whole of gestation exposure of fetal mouse brains to mobile phone radiofrequency fields did not produce any stress response using HSPs as an immunohistochemical marker.

(NE) Finnie JW, Cai Z, Manavis J, Helps S, Blumbergs PC. Microglial activation as a measure of stress in mouse brains exposed acutely (60 minutes) and long-term (2 years) to mobile telephone radiofrequency fields. Pathology. 42(2):151-154, 2010. (AS, CE, CC)

AIM: To determine whether acute or long-term exposure of the brain to mobile telephone radiofrequency (RF) fields produces activation of microglia, which normally respond rapidly to any change in their microenvironment. **METHODS:** Using a purpose designed exposure system at 900 MHz, mice were given a single, far-field whole body exposure at a specific absorption rate (SAR) of 4 W/kg for 60 min (acute) or on five successive days per week for 104 weeks (long-term). Control mice were sham-exposed or freely mobile in a cage to control for any stress caused by immobilisation in the exposure module. Positive control brains subjected to a stab wound were also included to confirm the ability of microglia to react to any neural stress. Brains were perfusion-fixed with 4% paraformaldehyde and representative regions of the cerebral cortex and hippocampus immunostained for ionised calcium binding adaptor molecule (Iba1), a specific microglial marker. **RESULTS:** There was no increase in microglial Iba1 expression in brains short or long-term exposed to mobile telephony microwaves compared to control (sham-exposed or freely moving caged mice) brains, while substantial microglial activation occurred in damaged positive control neural tissue. **CONCLUSION:** Acute (60 minutes) or longer duration (2 years) exposure of murine brains to mobile telephone RF fields did not produce any microglial activation detectable by Iba1 immunostaining.

(E) Fragopoulou AF, Miltiadous P, Stamatakis A, Stylianopoulou F, Koussoulakos SL, Margaritis LH. Whole body exposure with GSM 900MHz affects spatial memory in mice. Pathophysiology. 17(3):179-187, 2010. (AS, BE)

Extended work has been performed worldwide on the effects of mobile phone radiation upon rats' cognitive functions, however there is great controversy to the existence or not of deficits. The present work has been designed in order to test the effects of mobile phone radiation on spatial learning and memory in mice Mus musculus Balb/c using the Morris water maze (a hippocampal-dependent spatial memory task), since there is just one other study on mice with very low SAR level (0.05W/kg) showing no effects. We have applied a 2h daily dose of pulsed GSM 900MHz radiation from commercially available mobile phone for 4 days at SAR values ranging from 0.41 to 0.98W/kg. Statistical analysis revealed that during learning, exposed animals showed a deficit in transferring the acquired spatial information across training days (increased escape latency and distance swam, compared to the sham-exposed animals, on the first trial of training days 2-4). Moreover, during the memory probe-trial sham-exposed animals showed the expected preference for the target quadrant, while the exposed animals showed no preference, indicating that the exposed mice had deficits in consolidation and/or retrieval of the learned spatial information. Our results provide a basis for more thorough investigations considering reports on non-thermal effects of electromagnetic fields (EMFs).

(E) Fragopoulou AF, Samara A, Antonelou MH, Xanthopoulou A, Papadopoulou A, Vougas K, Koutsogiannopoulou E, Anastasiadou E, Stravopodis DJ, Tsangaris GT, Margaritis LH. Brain proteome response following whole body exposure of mice to mobile phone or wireless DECT base radiation. Electromagn Biol Med. 31(4):250-274, 2012. (AS, CE, CH, LI)

The objective of this study was to investigate the effects of two sources of electromagnetic fields (EMFs) on the proteome of cerebellum, hippocampus, and frontal lobe in Balb/c mice

following long-term whole body irradiation. Three equally divided groups of animals (6 animals/group) were used; the first group was exposed to a typical mobile phone, at a SAR level range of 0.17-0.37 W/kg for 3 h daily for 8 months, the second group was exposed to a wireless DECT base (Digital Enhanced Cordless Telecommunications/Telephone) at a SAR level range of 0.012-0.028 W/kg for 8 h/day also for 8 months and the third group comprised the sham-exposed animals. Comparative proteomics analysis revealed that long-term irradiation from both EMF sources altered significantly ($p < 0.05$) the expression of 143 proteins in total (as low as 0.003 fold downregulation up to 114 fold overexpression). Several neural function related proteins (i.e., Glial Fibrillary Acidic Protein (GFAP), Alpha-synuclein, Glia Maturation Factor beta (GMF), and apolipoprotein E (apoE)), heat shock proteins, and cytoskeletal proteins (i.e., Neurofilaments and tropomodulin) are included in this list as well as proteins of the brain metabolism (i.e., Aspartate aminotransferase, Glutamate dehydrogenase) to nearly all brain regions studied. Western blot analysis on selected proteins confirmed the proteomics data. The observed protein expression changes may be related to brain plasticity alterations, indicative of oxidative stress in the nervous system or involved in apoptosis and might potentially explain human health hazards reported so far, such as headaches, sleep disturbance, fatigue, memory deficits, and brain tumor long-term induction under similar exposure conditions.

(NE) Fritzer G, Göder R, Friege L, Wachter J, Hansen V, Hinze-Selch D, Aldenhoff JB. Effects of short- and long-term pulsed radiofrequency electromagnetic fields on night sleep and cognitive functions in healthy subjects. Bioelectromagnetics. 28(4):316-325, 2007. (HU, BE, EE, SL)

There has been wide public discussion on whether the electromagnetic fields of mobile telephones and their base stations affect human sleep or cognitive functioning. As there is evidence for learning and memory-consolidating effects of sleep and particularly of REM sleep, disturbance of sleep by radiofrequency electromagnetic fields might also impair cognitive functions. Previously realized sleep studies yielded inconsistent results regarding short-term exposure. Moreover, data are lacking on the effect that short- and long-term exposure might have on sleep as well as on cognitive functions. Therefore, 10 healthy young male subjects were included and nocturnal sleep was recorded during eight consecutive nights. In the second, third, and last night, we investigated polysomnographic night sleep and cognitive functions. After the adaptation and baseline nights, the participants were exposed to a defined radiofrequency electromagnetic field during the following six nights. We analyzed polysomnographic night sleep according to Rechtschaffen and Kales [1968, Manual of Standardized Terminology, Techniques and Scoring System for Sleep of Human Subjects] as well as by power spectra and correlation dimension. Cognitive functions were investigated by an array of neuropsychological tests. Data analysis was done by comparing the baseline night with the first and last exposure night and the first two sleep cycles of the respective nights. We did not find significant effects, either on conventional sleep parameters or on power spectra and correlation dimension, nor were there any significant effects on cognitive functions. With our results, we are unable to reveal either short-term or cumulative long-term effects of radiofrequency electromagnetic fields on night sleep and cognitive functions in healthy young male subjects.

(E) Furtado-Filho OV, Borba JB, Maraschin T, Souza LM, Jose JA, Moreira CF, Saffi J. Effects of chronic exposure to 950 MHz ultra-high-frequency electromagnetic radiation on reactive oxygen species metabolism in the right and left cerebral cortex of young rats of different ages. Int J Radiat Biol. 2015 Aug 14:1-17. [Epub ahead of print] (AS, CE, OX, CH, AD)

PURPOSE: To assess the effect of 950 MHz ultra-high-frequency electromagnetic radiation (UHF-EMR) on biomarkers of oxidative damage to DNA, proteins and lipids in the left cerebral cortex (LCC) and right cerebral cortex (RCC) of neonate and 6-day-old rats. MATERIALS AND METHODS: Twelve rats were equally divided into two groups as controls (CR) and exposed (ER), for each age (0 and 6 days). The LCC and RCC were examined in ER and CR after exposure. Radiation exposure lasted half an hour per day for up to 27 days (throughout pregnancy and 6 days postnatal). The specific absorption rate ranged from 1.32 - 1.14 W/kg. The damage to lipids, proteins and DNA was verified by thiobarbituric acid reactive substances, carbonylated proteins (CP) and comets, respectively. The concentration of glucose in the peripheral blood of the rats was measured by the Accu-Chek Active Kit due to increased CP in RCC. RESULTS: In neonates, no modification of the biomarkers tested was detected. On the other hand, there was an increase in the levels of CP in the RCC of the 6-day-old ER. Interestingly, the concentration of blood glucose was decreased in this group. CONCLUSIONS: Our results indicate that there is no genotoxicity and oxidative stress in neonates and 6 days rats. However, the RCC had the highest concentration of CP that do not seem to be a consequence of oxidative stress. This study is the first to demonstrate the use of UHF-EMR causes different damage responses to proteins in the LCC and RCC.

(E) Gao X, Luo R, Ma B, Wang H, Liu T, Zhang J, Lian Z, Cui X. [Interference of vitamin E on the brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats]. Wei Sheng Yan Jiu. 42(4):642-646, 2013.[Article in Chinese] **(AS, CE, ME, OX, DE)**

OBJECTIVE: To investigate the interlerence ot vitamin E on brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats. METHODS: 40 pregnant rats were randomly divided into five groups (positive control, negative control, low, middle and high dosage of vitamin E groups). The low, middle and high dosage of vitamin E groups were supplemented with 5, 15 and 30 mg/ml vitamin E respectively since the first day of pregnancy. And the negative control group and the positive control group were given peanut oil without vitamin E. All groups except for the negative control group were exposed to 900MHz intensity of cell phone radiation for one hour each time, three times per day for 21 days. After accouchement, the right hippocampus tissue of fetal rats in each group was taken and observed under electron microscope. The vitality of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and the content of malondialdehyde (MDA) in pregnant and fetal rats' brain tissue were tested. RESULTS: Compared with the negative control group, the chondriosomes in neuron and neuroglia of brain tissues was swelling, mild edema was found around the capillary, chromatin was concentrated and collected, and bubbles were formed in vascular endothelial cells (VEC) in the positive fetal rat control group, whereas the above phenomenon was un-conspicuous in the middle and high dosage of vitamin E groups. We can

see uniform chromatin, abundant mitochondrion, rough endoplasmic reticulum and free ribosomes in the high dosage group. The apoptosis has not found in all groups'sections. In the antioxidase activity analysis, compared with the negative control group, the vitality of SOD and GSH-Px significantly decreased and the content of MDA significantly increased both in the pregnant and fetal rats positive control group ($P < 0.05$). In fetal rats, the vitality of SOD and GSH-Px significantly increased in the brain tissues of all three different vitamin E dosages groups when compared with the positive control group, and the content of MDA was found significantly decreased in both middle and high dosage of vitamin E groups($P < 0.05$). The same results have also been found in high dosage pregnant rat group, but in middle dosage group only SOD activity was found increased with significance ($P < 0.05$). With the dosage increase of vitamin E, the vitality of SOD and GSH-Px was increasing and the content of MDA was decreasing. CONCLUSION: Under the experimental dosage, vitamin E has certain interference on damage of antioxidant capacity and energy metabolization induced by electromagnetic radiation of cell phone in pregnant rats and fetal rats.

(E) Geronikolou SA, Chamakou A, Mantzou A, Chrousos G, KanakaGantenbein C. Frequent cellular phone use modifies hypothalamic-pituitary-adrenal axis response to a cellular phone call after mental stress in healthy children and adolescents: A pilot study. Sci Total Environ. 536:182-188, 2015. (HU, BE, PE)

OBJECTIVE: The hypothalamic-pituitary-adrenal (HPA) axis is the main "gate-keeper" of the organism's response to every somatic or mental stress. This prospective study aims to investigate the HPA-axis response to a cellular phone call exposure after mental stress in healthy children and adolescents and to assess the possible predictive role of baseline endocrine markers to this response. SUBJECTS AND METHODS: Two groups of healthy school-age children aged 11-14 (12.5±1.5) years were included in the study, the one comprising those who are occasional users of a cellular phone (Group A; n=16)) while the second those who do regularly use one (Group B; n=12). Blood samples were obtained from all participants at 8.00am after a 12-hour overnight fasting for thyroid hormone, glucose, insulin, and cortisol levels determination. The participants performed the Trier Social Stress Test for Children (TSST-C) (5 min oral task followed by 5min arithmetic task). Salivary cortisol samples were obtained at baseline, 10 and 20 min after the TSST-C and 10 and 20 min after a 5-minute cellular phone call. RESULTS: Significant changes in the salivary cortisol levels were noted between 10 and 20 mins after the cellular phone call with different responses between the two groups. Baseline thyroid hormone levels seem to predict the cortisol response to mental stress mainly in group A, while HOMA (homostasis model assessment) had no impact on salivary cortisol response at any phase of the test, in either group. CONCLUSIONS: HPA axis response to cellular phone after mental stress in children and adolescents follow a different pattern in frequent users than in occasional users that seems to be influenced by the baseline thyroid hormone levels.

(E) Gevrek F. Histopathological, immunohistochemical, and stereological analysis of the effect of Gingko biloba (Egb761) on the hippocampus of rats exposed to long-term cellphone radiation. Histol Histopathol. 2017 Nov 9:11943. (AS, CE, CC, CH)

Cellular phones are major sources of electromagnetic radiation (EMR) that can penetrate the human body and pose serious health hazards. The increasingly widespread use of mobile communication systems has raised concerns about the effects of cellphone radiofrequency (RF) on the hippocampus because of its close proximity to radiation during cellphone use. The effects of cellphone EMR exposure on the hippocampus of rats and the possible counteractive effects of ginkgo biloba (Egb761) were aimed to investigate. Rats were divided into three groups: Control, EMR, and EMR+Egb761. The EMR and EMR+Egb761 groups were exposed to cellphone EMR for one month. Egb761 was also administered to the EMR+Egb761 group. Specifically, we evaluated the effect of RF exposure on rat hippocampi at harmful EMR levels (0.96 W/kg specific absorption rate [SAR]) for one month and also investigated the possible impact of ginkgo biloba (Egb761) using stereological, TUNEL-staining, and immunohistochemical methods. An increase in apoptotic proteins (Bax, Acas-3) and a decrease in anti-apoptotic protein (Bcl-2) immunoreactivity along with a decrease in the total granule and pyramidal cell count were noted in the EMR group. A decrease in Bax and Acas-3 and an increase in Bcl-2 immunoreactivity were observed in rats treated with Egb761 in addition to a decrease in TUNEL-stained apoptotic cells and a higher total viable cell number. In conclusion, chronic cellphone EMR exposure may affect hippocampal cell viability, and Egb761 may be used to mitigate some of the deleterious effects.

(E) Ghazizadeh V, Nazıroğlu M. Electromagnetic radiation (Wi-Fi) and epilepsy induce calcium entry and apoptosis through activation of TRPV1 channel in hippocampus and dorsal root ganglion of rats. Metab Brain Dis. 2014 May 3. [Epub ahead of print] (AS, CC, CH, OX)

Incidence rates of epilepsy and use of Wi-Fi worldwide have been increasing. TRPV1 is a Ca^{2+} permeable and non-selective channel, gated by noxious heat, oxidative stress and capsaicin (CAP). The hyperthermia and oxidant effects of Wi-Fi may induce apoptosis and Ca^{2+} entry through activation of TRPV1 channel in epilepsy. Therefore, we tested the effects of Wi-Fi (2.45 GHz) exposure on Ca^{2+} influx, oxidative stress and apoptosis through TRPV1 channel in the murine dorsal root ganglion (DRG) and hippocampus of pentylentetrazol (PTZ)-induced epileptic rats. Rats in the present study were divided into two groups as controls and PTZ. The PTZ groups were divided into two subgroups namely PTZ + Wi-Fi and PTZ + Wi-Fi + capsazepine (CPZ). The hippocampal and DRG neurons were freshly isolated from the rats. The DRG and hippocampus in PTZ + Wi-Fi and PTZ + Wi-Fi + CPZ groups were exposed to Wi-Fi for 1 hour before CAP stimulation. The cytosolic free Ca^{2+}, reactive oxygen species production, apoptosis, mitochondrial membrane depolarization, caspase-3 and -9 values in hippocampus were higher in the PTZ group than in the control although cell viability values decreased. The Wi-Fi exposure induced additional effects on the cytosolic Ca^{2+} increase. However, pretreatment of the neurons with CPZ, results in a protection against epilepsy-induced Ca^{2+} influx, apoptosis and oxidative damages. In results of whole cell patch-clamp experiments, treatment of DRG with Ca^{2+} channel antagonists [thapsigargin, verapamil + diltiazem, 2-APB, MK-801] indicated that Wi-Fi exposure induced Ca^{2+} influx via the TRPV1 channels. In conclusion, epilepsy and Wi-Fi in our experimental model is involved in Ca^{2+} influx and oxidative stress-induced hippocampal and DRG death through activation of TRPV1 channels, and negative modulation of this channel

activity by CPZ pretreatment may account for the neuroprotective activity against oxidative stress.

(E) Ghosn R, Yahia-Cherif L, Hugueville L, Ducorps A, Lemaréchal JD, Thuróczy G, de Seze R, Selmaoui B. Radiofrequency signal affects alpha band in resting electroencephalogram. J Neurophysiol. 113(7):2753-2759, 2015. (HU, EE)

The aim of the present work was to investigate the effects of the radiofrequency (RF) electromagnetic fields (EMFs) on human resting EEG with a control of some parameters that are known to affect alpha band, such as electrode impedance, salivary cortisol, and caffeine. Eyes-open and eyes-closed resting EEG data were recorded in 26 healthy young subjects under two conditions: sham exposure and real exposure in double-blind, counterbalanced, crossover design. Spectral power of EEG rhythms was calculated for the alpha band (8-12 Hz). Saliva samples were collected before and after the study. Salivary cortisol and caffeine were assessed by ELISA and HPLC, respectively. The electrode impedance was recorded at the beginning of each run. Compared with the sham session, the exposure session showed a statistically significant ($P < 0.0001$) decrease of the alpha band spectral power during closed-eyes condition. This effect persisted in the postexposure session ($P < 0.0001$). No significant changes were detected in electrode impedance, salivary cortisol, and caffeine in the sham session compared with the exposure one. These results suggest that GSM-EMFs of a mobile phone affect the alpha band within spectral power of resting human EEG.

(E) Gökçek-Saraç Ç, Er H, Kencebay Manas C, Kantar Gok D, Özen Ş, Derin N. Effects of acute and chronic exposure to both 900 MHz and 2100 MHz electromagnetic radiation on glutamate receptor signaling pathway. Int J Radiat Biol. 93(9):980-989, 2017. (AC, CE, CC, CH)

PURPOSE: To demonstrate the molecular effects of acute and chronic exposure to both 900 and 2100 MHz radiofrequency electromagnetic radiation (RF-EMR) on the hippocampal level/activity of some of the enzymes - including PKA, CaMKIIα, CREB, and p44/42 MAPK - from N-methyl-D-aspartate receptor (NMDAR)-related signaling pathways. **MATERIALS AND METHODS:** Rats were divided into the following groups: sham rats, and rats exposed to 900 and 2100 MHz RF-EMR for 2 h/day for acute (1 week) or chronic (10 weeks), respectively. Western blotting and activity measurement assays were used to assess the level/activity of the selected enzymes. **RESULTS:** The obtained results revealed that the hippocampal level/activity of selected enzymes was significantly higher in the chronic groups as compared to the acute groups at both 900 and 2100 MHz RF-EMR exposure. In addition, hippocampal level/activity of selected enzymes was significantly higher at 2100 MHz RF-EMR than 900 MHz RF-EMR in both acute and chronic groups. **CONCLUSIONS:** The present study provides experimental evidence that both exposure duration (1 week versus 10 weeks) and different carrier frequencies (900 vs. 2100 MHz) had different effects on the protein expression of hippocampus in Wistar rats, which might encourage further research on protection against RF-EMR exposure.

(NE) Grafström G, Nittby H, Brun A, Malmgren L, Persson BR, Salford LG, Eberhardt J. Histopathological examinations of rat brains after long-term exposure to GSM-900 mobile phone radiation. Brain Res Bull. 77(5):257-263, 2008. (AS, CE, ME, CH, LI)

In order to mimic the real life situation, with often life-long exposure to the electromagnetic fields emitted by mobile phones, we have investigated in a rat model the effects of repeated exposures under a long period to Global System for Mobile Communication-900 MHz (GSM-900) radiation. Out of a total of 56 rats, 32 were exposed once weekly in a 2-h period, for totally 55 weeks, at different average whole-body specific absorption rates (SAR) (of in average 0.6 and 60 mW/kg at the initiation of the experimental period). The animals were exposed in a transverse electromagnetic transmission line chamber (TEM-cell) to radiation emitted by a GSM-900 test phone. Sixteen animals were sham exposed and eight animals were cage controls, which never left the animal house. After behavioural tests, 5-7 weeks after the last exposure, the brains were evaluated for histopathological alterations such as albumin extravasation, dark neurons, lipofuscin aggregation and signs of cytoskeletal and neuritic neuronal changes of the type seen in human ageing. In this study, no significant alteration of any these histopathological parameters was found, when comparing the GSM exposed animals to the sham exposed controls.

(NE) Gupta N, Goyal D, Sharma R, Arora KS. Effect of Prolonged Use of Mobile Phone on Brainstem Auditory Evoked Potentials. J Clin Diagn Res. 9(5):CC07-9, 2015. (HU, CE, EE)

OBJECTIVES: Mobile phones are being widely used throughout the world. Electromagnetic waves generated from mobile phones have raised concerns as these may have adverse effects on human auditory system owing to the daily use of mobile phones. The purpose of current study was to evaluate the effects of long term mobile phone usage on auditory brainstem evoked responses (ABR). MATERIALS AND METHODS: A retrospective, cross-sectional, case control study was carried out in a tertiary care hospital. Total 100 healthy subjects aged 18 to 30 years of both the genders were selected, out of which 67 subjects were long-term GSM mobile phone users (using mobile phone for more than 1 year) and 33 were controls who were mobile phone non users. Both the groups were investigated for ABR and changes were studied in both the ears of cases and controls to ascertain the effects of electromagnetic exposure. RESULTS: No significant difference ($p>0.05$) was found in latencies, interpeak latencies and amplitudes of ABR waves between cases and controls. CONCLUSION: Our study shows that long term usage of mobile phones does not affect propagation of electrical stimuli along the auditory nerve to auditory brainstem centres.

(NE) Guxens M, van Eijsden M, Vermeulen R, Loomans E, Vrijkotte TG, Komhout H, van Strien RT, Huss A. Maternal cell phone and cordless phone use during pregnancy and behaviour problems in 5-year-old children. J Epidemiol Community Health. 2013 Feb 5. [Epub ahead of print] (HU, DE, BE)

BACKGROUND: A previous study found an association between maternal cell phone use during pregnancy and maternal-reported child behaviour problems at age 7. Together with cell phones, cordless phones represent the main exposure source of radiofrequency-electromagnetic fields to the head. Therefore, we assessed the association between maternal cell phone and cordless phone use during pregnancy and teacher-reported and maternal-reported child behaviour problems at age 5. **METHODS:** The study was embedded in the Amsterdam Born Children and their Development study, a population-based birth cohort study in Amsterdam, the Netherlands (2003-2004). Teachers and mothers reported child behaviour problems using the Strength and Difficulties Questionnaire at age 5. Maternal cell phone and cordless phone use during pregnancy was asked when children were 7 years old. **RESULTS:** A total of 2618 children were included. As compared to non-users, those exposed to prenatal cell phone use showed an increased but non-significant association of having teacher-reported overall behaviour problems, although without dose-response relationship with the number of calls (OR=2.12 (95% CI 0.95 to 4.74) for <1 call/day, OR=1.58 (95% CI 0.69 to 3.60) for 1-4 calls/day and OR=2.04 (95% CI 0.86 to 4.80) for ≥5 calls/day). ORs for having teacher-reported overall behaviour problems across categories of cordless phone use were below 1 or close to unity. Associations of maternal cell phone and cordless phone use with maternal-reported overall behaviour problems remained non-significant. Non-significant associations were found for the specific behaviour problem subscales. **CONCLUSION:** Our results do not suggest that maternal cell phone or cordless phone use during pregnancy increases the odds of behaviour problems in their children.

(NE) Haarala C, Takio F, Rintee T, Laine M, Koivisto M, Revonsuo A, Hämäläinen H. Pulsed and continuous wave mobile phone exposure over left versus right hemisphere: effects on human cognitive function. Bioelectromagnetics. 28(4):289-295, 2007. (HU, BE)

The possible effects of continuous wave (CW) and pulse modulated (PM) electromagnetic field (EMF) on human cognition was studied in 36 healthy male subjects. They performed cognitive tasks while exposed to CW, PM, and sham EMF. The subjects performed the same tasks twice during each session; once with left-sided and once with right-sided exposure. The EMF conditions were spread across three testing sessions, each session separated by 1 week. The exposed hemisphere, EMF condition, and test order were counterbalanced over all subjects. We employed a double-blind design: both the subject and the experimenter were unaware of the EMF condition. The EMF was created with a signal generator connected via amplifier to a dummy phone antenna, creating a power output distribution similar to the original commercial mobile phone. The EMF had either a continuous power output of 0.25 W (CW) or pulsed power output with a mean of 0.25 W. An additional control group of 16 healthy male volunteers performed the same tasks without any exposure equipment to see if mere presence of the equipment could have affected the subjects' performance. No effects were found between the different EMF conditions, separate hemisphere exposures, or between the control and experimental group. In conclusion, the current results indicate that normal mobile phones have no discernible effect on human cognitive function as measured by behavioral tests.

(E) Haghani M, Shabani M, Moazzami K. Maternal mobile phone exposure adversely affects the electrophysiological properties of Purkinje neurons in rat offspring. Neuroscience. 2013 Jul 29. pii: S0306-4522(13)00643-X. doi: 10.1016/j.neuroscience.2013.07.049. [Epub ahead of print] (AS, CE, EE, CC, DE) no behavioral effect.

Electromagnetic field (EMF) radiations emitted from mobile phones may cause structural damage to neurons. With the increased usage of mobile phones worldwide, concerns about their possible effects on the nervous system are rising. In the present study, we aimed to elucidate the possible effects of prenatal EMF exposure on the cerebellum of offspring Wistar rats. Rats in EMF group were exposed to 900 MHz Pulse-EMF irradiation for six hours per day during all gestation period. Ten offspring's per each group were evaluated for behavioral and electrophysiological evaluations. Cerebellum - related behavioral dysfunctions were analyzed using motor learning and cerebellum-dependent functional tasks (Accelerated Rotarod, Hanging and Open field tests). Whole cell- patch clamp recordings were used for electrophysiological evaluations. The results of the present study failed to show any behavioral abnormalities in rats exposed to chronic EMF radiation. However, whole cell patch clamp recordings revealed decreased neuronal excitability of Purkinje cells in rats exposed to EMF. The most prominent changes included afterhyperpolarization amplitude, spike frequency, half width and first spike latency. In conclusion, the results of the present study show that prenatal EMF exposure results in altered electrophysiological properties of Purkinje neurons. However, these changes may not be severe enough to alter the cerebellum-dependent functional tasks.

(E) Hao D, Yang L, Chen S, Tong J, Tian Y, Su B, Wu S, Zeng Y. Effects of long-term electromagnetic field exposure on spatial learning and memory in rats. Neurol Sci. 34:157-164, 2013. (AS, CE, BE, CC, EE)

With the development of communications industry, mobile phone plays an important role in daily life. Whether or not the electromagnetic radiation emitted by mobile phone causes any adverse effects on brain function has become of a great concern. This paper investigated the effect of electromagnetic field on spatial learning and memory in rats. 32 trained Wistar rats were divided into two groups: exposure group and control group. The exposure group was exposed to 916 MHz, 10w/m2 mobile phone electromagnetic field (EMF) 6 h a day, 5 days a week, 10 weeks. The completion time, number of total errors and the neuron discharge signals were recorded while the rats were searching for food in an eight-arm radial maze at every weekend. The neuron signals of one exposed rat and one control rat in the maze were obtained by the implanted microelectrode arrays in their hippocampal regions. It can be seen that during the weeks 4-5 of the experiment, the average completion time and error rate of the exposure group were longer and larger than that of control group ($p < 0.05$). During the weeks 1-3 and 6-9, they were close to each other. The hippocampal neurons showed irregular firing patterns and more spikes with shorter interspike interval during the whole experiment period. It indicates that the 916 MHz EMF influence learning and memory in rats to some extent in a period during exposure, and the rats can adapt to long-term EMF exposure.

(E) Hao Y, Yang X, Chen C, Yuan-Wang, Wang X, Li M, Yu Z. STAT3 signalling pathway is involved in the activation of microglia induced by 2.45 GHz electromagnetic fields. Int J Radiat Biol. 86(1):27-36, 2010. (CS, CH, OX)

PURPOSE: Microglia activation plays a pivotal role in the initiation and progression of central nervous system (CNS) insult. The aim of the present work was to investigate the activation of microglia and involvement of signal transducer and activator of transcription 3 (STAT3) in microglia activation after 2.45 GHz electromagnetic fields (EMF) exposure. **MATERIALS AND METHODS:** In this study, murine N9 microglial cells were exposed to 2.45 GHz EMF, the protein expressions of STAT3, Janus Tyrosine kinase 1 and 2(JAK1 and JAK2), phosphor-(Try705)STAT3 and DNA binding activity of STAT3 were examined by Western blot analysis and electrophoresis mobility shift assay (EMSA). Levels of the nitric oxide (NO) derivative nitrite were determined in the culture medium by the Griess reaction. The mRNA expression of tumour necrosis factor alpha (TNF-alpha) and inducible nitric oxide synthase (iNOS) were detected by reverse transcription and polymerase chain reaction (RT-PCR). **RESULTS:** A significant increase of STAT3 DNA-binding ability was noted after exposure. Consistent with this, EMF rapidly induced phosphorylation of STAT3 and activated JAK1 and JAK2. In addition, EMF exposure increased transcription levels of the inflammation-associated genes, iNOS and TNF-alpha, which are reported to contain STAT-binding elements in their promoter region. P6, a JAK inhibitor, reduced induction of iNOS and TNF-alpha, nuclear factor binding activity, and activation of STAT3 in EMF-stimulated microglia. **CONCLUSION:** These results provide evidence that EMF exposure can initiate the activation of microglia cells and STAT3 signalling involves in EMF-induced microglial activation.

(E) Hardell L, Söderqvist F, Carlberg M, Zetterberg H, Mild KH. Exposure to wireless phone emissions and serum beta-trace protein. Int J Mol Med. 26(2):301-306, 2010. (HU, CH, SL)

The lipocalin type of prostaglandin D synthase or beta-trace protein is synthesized in the choroid plexus, lepto-meninges and oligodendrocytes of the central nervous system and is secreted into the cerebrospinal fluid. beta-trace protein is the key enzyme in the synthesis of prostaglandin D2, an endogenous sleep-promoting neurohormone in the brain. Electromagnetic fields (EMF) in the radio frequency (RF) range have in some studies been associated with disturbed sleep. We studied the concentration of beta-trace protein in blood in relation to emissions from wireless phones. This study included 62 persons aged 18-30 years. The concentration of beta-trace protein decreased with increasing number of years of use of a wireless phone yielding a negative beta coefficient = -0.32, 95% confidence interval -0.60 to -0.04. Also cumulative use in hours gave a negative beta coefficient, although not statistically significant. Of the 62 persons, 40 participated in an experimental study with 30 min exposure to an 890-MHz GSM signal. No statistically significant change of beta-trace protein was found. In a similar study of the remaining 22 participitants with no exposure, beta-trace protein increased significantly over time, probably due to a relaxed situation. EMF emissions may down-regulate the synthesis of beta-trace protein. This mechanism might be involved in sleep disturbances reported in persons exposed to RF fields. The results must be interpreted with caution since use

of mobile and cordless phones were self-reported. Awareness of exposure condition in the experimental study may have influenced beta-trace protein concentrations.

(NE) Hareuveny R, Eliyahu I, Luria R, Meiran N, Margaliot M. Cognitive effects of cellular phones: a possible role of non-radiofrequency radiation factors. Bioelectromagnetics. 32(7):585-588, 2011. (See also: Luria et al., 2009) (HU, BE)

Some studies found that cognitive functions of human beings may be altered while exposed to radiofrequency radiation (RFR) emitted by cellular phones. In two recent studies, we have found that experiment duration and exposure side (i.e., phone's location--right or left) may have a major influence on the detection of such effects. In this brief follow-up experiment, 29 right-handed male subjects were divided into two groups. Each subject had two standard cellular phones attached to both sides of his head. The subjects performed a spatial working memory task that required either a left-hand or a right-hand response under one of the two exposure conditions: left side of the head or right side. Contrary to our previous studies, in this work external antennas located far away from the subjects were connected to the cellular phones. This setup prevents any emission of RFR from the internal antenna, thus drastically reducing RFR exposure. Despite that, the results remain similar to those obtained in our previous work. These results indicate that some of the effects previously attributed to RFR can be the result of some confounders.

(E) Hassanshahi A, Shafeie SA, Fatemi I, Hassanshahi E, Allahtavakoli M, Shabani M, Roohbakhsh A, Shamsizadeh A. The effect of Wi-Fi electromagnetic waves in unimodal and multimodal object recognition tasks in male rats. Neurol Sci. 2017 Mar 22. doi: 10.1007/s10072-017-2920-y. [Epub ahead of print] (AS, CE, BE, CC)

Wireless internet (Wi-Fi) electromagnetic waves (2.45 GHz) have widespread usage almost everywhere, especially in our homes. Considering the recent reports about some hazardous effects of Wi-Fi signals on the nervous system, this study aimed to investigate the effect of 2.4 GHz Wi-Fi radiation on multisensory integration in rats. This experimental study was done on 80 male Wistar rats that were allocated into exposure and sham groups. Wi-Fi exposure to 2.4 GHz microwaves [in Service Set Identifier mode (23.6 dBm and 3% for power and duty cycle, respectively)] was done for 30 days (12 h/day). Cross-modal visual-tactile object recognition (CMOR) task was performed by four variations of spontaneous object recognition (SOR) test including standard SOR, tactile SOR, visual SOR, and CMOR tests. A discrimination ratio was calculated to assess the preference of animal to the novel object. The expression levels of M1 and GAT1 mRNA in the hippocampus were assessed by quantitative real-time RT-PCR. Results demonstrated that rats in Wi-Fi exposure groups could not discriminate significantly between the novel and familiar objects in any of the standard SOR, tactile SOR, visual SOR, and CMOR tests. The expression of M1 receptors increased following Wi-Fi exposure. In conclusion, results of this study showed that chronic

exposure to Wi-Fi electromagnetic waves might impair both unimodal and cross-modal encoding of information.

(E) He GL, Luo Z, Shen TT, Li P, Yang J, Luo X, Chen CH, Gao P, Yang XS. Inhibition of STAT3- and MAPK-dependent PGE2 synthesis ameliorates phagocytosis of fibrillar β-amyloid peptide (1-42) via EP2 receptor in EMF-stimulated N9 microglial cells. J Neuroinflammation. 13(1):296, 2016. (CS, CH)

BACKGROUND: Prostaglandin E_2 (PGE_2)-involved neuroinflammatory processes are prevalent in several neurological conditions and diseases. Amyloid burden is correlated with the activation of E-prostanoid (EP) 2 receptors by PGE_2 in Alzheimer's disease. We previously demonstrated that electromagnetic field (EMF) exposure can induce pro-inflammatory responses and the depression of phagocytosis in microglial cells, but the signaling pathways involved in phagocytosis of fibrillar β-amyloid (fAβ) in microglial cells exposed to EMF are poorly understood. Given the important role of PGE_2 in neural physiopathological processes, we investigated the PGE_2-related signaling mechanism in the immunomodulatory phagocytosis of EMF-stimulated N9 microglial cells (N9 cells). **METHODS:** N9 cells were exposed to EMF with or without pretreatment with the selective inhibitors of cyclooxygenase-2 (COX-2), Janus kinase 2 (JAK2), signal transducer and activator of transcription 3 (STAT3), and mitogen-activated protein kinases (MAPKs) and antagonists of PG receptors EP1-4. The production of endogenous PGE_2 was quantified by enzyme immunoassays. The phagocytic ability of N9 cells was evaluated based on the fluorescence intensity of the engulfed fluorescent-labeled fibrillar β-amyloid peptide (1-42) ($fA\beta_{42}$) measured using a flow cytometer and a fluorescence microscope. The effects of pharmacological agents on EMF-activated microglia were investigated based on the expressions of JAK2, STAT3, p38/ERK/JNK MAPKs, COX-2, microsomal prostaglandin E synthase-1 (mPGES-1), and EP2 using real-time PCR and/or western blotting. **RESULTS:** EMF exposure significantly increased the production of PGE_2 and decreased the phagocytosis of fluorescent-labeled $fA\beta_{42}$ by N9 cells. The selective inhibitors of COX-2, JAK2, STAT3, and MAPKs clearly depressed PGE_2 release and ameliorated microglial phagocytosis after EMF exposure. Pharmacological agents suppressed the phosphorylation of JAK2-STAT3 and MAPKs, leading to the amelioration of the phagocytic ability of EMF-stimulated N9 cells. Antagonist studies of EP1-4 receptors showed that EMF depressed the phagocytosis of $fA\beta_{42}$ through the PGE_2 system, which is linked to EP2 receptors.**CONCLUSIONS:** This study indicates that EMF exposure could induce phagocytic depression via JAK2-STAT3- and MAPK-dependent PGE_2-EP2 receptor signaling pathways in microglia. Therefore, pharmacological inhibition of PGE_2 synthesis and EP2 receptors may be a potential therapeutic strategy to combat the neurobiological deterioration that follows EMF exposure.

(NE) Heinrich S, Thomas S, Heumann C, von Kries R, Radon K. Association between exposure to radiofrequency electromagnetic fields assessed by dosimetry and acute symptoms in children and adolescents: a population based cross-sectional study. Environ Health. 9:75, 2010. (HU, BE)

BACKGROUND: The increase in numbers of mobile phone users was accompanied by some concern that exposure to radiofrequency electromagnetic fields (RF EMF) might adversely affect acute health especially in children and adolescents. The authors investigated this potential association using personal dosimeters. METHODS: A 24-hour exposure profile of 1484 children and 1508 adolescents was generated in a population-based cross-sectional study in Germany between 2006 and 2008 (participation 52%). Personal interview data on socio-demographic characteristics, self-reported exposure and potential confounders were collected. Acute symptoms were assessed twice during the study day using a symptom diary. RESULTS: Only few of the large number of investigated associations were found to be statistically significant. At noon, adolescents with a measured exposure in the highest quartile during morning hours reported a statistically significant higher intensity of headache (Odd Ratio: 1.50; 95% confidence interval: 1.03, 2.19). At bedtime, adolescents with a measured exposure in the highest quartile during afternoon hours reported a statistically significant higher intensity of irritation in the evening (4th quartile 1.79; 1.23, 2.61), while children reported a statistically significant higher intensity of concentration problems (4th quartile 1.55; 1.02, 2.33). *CONCLUSIONS: We observed few statistically significant results which are not consistent over the two time points.* Furthermore, when the 10% of the participants with the highest exposure are taken into consideration the significant results of the main analysis could not be confirmed. Based on the pattern of these results, we assume that the few observed significant associations are not causal but rather occurred by chance.

(E) Hidisoglu E, Kantar Gok D, Er H, Akpinar D, Uysal F, Akkoyunlu G, Ozen S, Agar A, Yargicoglu P. 2100-MHz electromagnetic fields have different effects on visual evoked potentials and oxidant/antioxidant status depending on exposure duration. Brain Res. 2016 Jan 14. pii: S0006-8993(16)00031-7. doi: 10.1016/j.brainres.2016.01.018. [Epub ahead of print] (AS, CE, EE, OX)

The purpose of the present study was to investigate the duration effects of 2100-MHz electromagnetic field (EMF) on visual evoked potentials (VEPs) and to assess lipid peroxidation (LPO), nitric oxide (NO) production and antioxidant status of EMF exposed rats. Rats were randomized to following groups: Sham rats (S1 and S10) and rats exposed to 2100-MHz EMF (E1 and E10) for 2h/day for 1 or 10 weeks, respectively. At the end of experimental periods, VEPs were recorded under anesthesia. Brain thiobarbituric acid reactive substances (TBARS) and 4-hydroxy-2-nonenal (4-HNE) levels were significantly decreased in the E1 whereas increased in the E10 compared with their control groups. While brain catalase (CAT), glutathione peroxidase (GSH-Px) activities and NO and glutathione (GSH) levels were significantly increased in the E1, reduction of superoxide dismutase (SOD) activity was detected in the same group compared with the S1. Conversely, decreased CAT, GSH-Px activities and NO levels were observed in the E10 compared with the S10. Latencies of all VEP components were shortened in the E1 compared with the S1, whereas latencies of all VEP components, except P1, were prolonged in the E10 compared with the S10. There was a positive correlation between all VEP latencies and brain TBARS and 4-HNE values. Consequently, it could be concluded that different effects of EMFs on VEPs depend on exposure duration. Additionally, our results indicated that short-term

EMF could provide protective effects, while long-term EMF could have an adverse effect on VEPs and oxidant/antioxidant status.

(NE) Hirose H, Sakuma N, Kaji N, Nakayama K, Inoue K, Sekijima M, Nojima T, Miyakoshi J. Mobile phone base station-emitted radiation does not induce phosphorylation of Hsp27. Bioelectromagnetics. 28(2):99-108, 2007. (CS, CH, LI)

An in vitro study focusing on the effects of low-level radiofrequency (RF) fields from mobile radio base stations employing the International Mobile Telecommunication 2000 (IMT-2000) cellular system was conducted to test the hypothesis that modulated RF fields act to induce phosphorylation and overexpression of heat shock protein hsp27. First, we evaluated the responses of human cells to microwave exposure at a specific absorption rate (SAR) of 80 mW/kg, which corresponds to the limit of the average whole-body SAR for general public exposure defined as a basic restriction in the International Commission on Non-Ionizing Radiation Protection (ICNIRP) guidelines. Second, we investigated whether continuous wave (CW) and Wideband Code Division Multiple Access (W-CDMA) modulated signal RF fields at 2.1425 GHz induced activation or gene expression of hsp27 and other heat shock proteins (hsps). Human glioblastoma A172 cells were exposed to W-CDMA radiation at SARs of 80 and 800 mW/kg for 2-48 h, and CW radiation at 80 mW/kg for 24 h. Human IMR-90 fibroblasts from fetal lungs were exposed to W-CDMA at 80 and 800 mW/kg for 2 or 28 h, and CW at 80 mW/kg for 28 h. Under the RF field exposure conditions described above, no significant differences in the expression levels of phosphorylated hsp27 at serine 82 (hsp27[pS82]) were observed between the test groups exposed to W-CDMA or CW signal and the sham-exposed negative controls, as evaluated immediately after the exposure periods by bead-based multiplex assays. Moreover, no noticeable differences in the gene expression of hsps were observed between the test groups and the negative controls by DNA Chip analysis. Our results confirm that exposure to low-level RF field up to 800 mW/kg does not induce phosphorylation of hsp27 or expression of hsp gene family.

(NE) Hirose H, Sasaki A, Ishii N, Sekijima M, Iyama T, Nojima T, Ugawa Y. 1950 MHz IMT-2000 field does not activate microglial cells in vitro. Bioelectromagnetics. 31(2):104-112, 2010. (CS, CC)

Given the widespread use of the cellular phone today, investigation of potential biological effects of radiofrequency (RF) fields has become increasingly important. In particular, much research has been conducted on RF effects on brain function. To examine any biological effects on the central nervous system (CNS) induced by 1950 MHz modulation signals, which are controlled by the International Mobile Telecommunication-2000 (IMT-2000) cellular system, we investigated the effect of RF fields on microglial cells in the brain. We assessed functional changes in microglial cells by examining changes in immune reaction-related molecule expression and cytokine production after exposure to a 1950 MHz Wideband Code Division Multiple Access (W-CDMA) RF field, at specific absorption rates (SARs) of 0.2, 0.8, and 2.0 W/kg. Primary microglial cell cultures prepared from neonatal rats were subjected to an RF or sham field for 2 h. Assay samples obtained 24 and 72 h after exposure were processed in a blind

manner. Results showed that the percentage of cells positive for major histocompatibility complex (MHC) class II, which is the most common marker for activated microglial cells, was similar between cells exposed to W-CDMA radiation and sham-exposed controls. No statistically significant differences were observed between any of the RF field exposure groups and the sham-exposed controls in percentage of MHC class II positive cells. Further, no remarkable differences in the production of tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), and interleukin-6 (IL-6) were observed between the test groups exposed to W-CDMA signal and the sham-exposed negative controls. These findings suggest that exposure to RF fields up to 2 W/kg does not activate microglial cells in vitro.

(E) Hountala CD, Maganioti AE, Papageorgiou CC, Nanou ED, Kyprianou MA, Tsiafakis VG, Rabavilas AD, Capsalis CN. The spectral power coherence of the EEG under different EMF conditions. Neurosci Lett. 441(2):188-192, 2008. (HU, EE)

The present study introduces the concept of spectral power coherence (SPC), which reflects the pattern of coordination of the four basic EEG bands (delta, theta, alpha, and beta) at a specific location of the brain. The SPC was calculated for the pre-stimulus EEG signal during an auditory memory task under different electromagnetic field (EMF) conditions (900 MHz and 1800 MHz). The results showed that delta rhythm is less consequential in the overall cooperation between the bands than the higher frequency theta, alpha and beta rhythms. Additionally, it has been shown that the radiation effect on SPC is different for the two genders. In the absence of radiation males exhibit higher overall SPC than females. These differences disappear in the presence of 900 MHz and are reversed in the presence of 1800 MHz.

(E) Hu S, Peng R, Wang C, Wang S, Gao Y, Dong J, Zhou H, Su Z, Qiao S, Zhang S, Wang L, Wen X.Neuroprotective effects of dietary supplement Kang-fu-ling against high-power microwave through antioxidant action. Food Funct. 2014 Jul 24. [Epub ahead of print] (AS, CE, CE, BE, ME, OX, IA)

Kang-fu-ling (KFL) is a polybotanical dietary supplement with antioxidant properties. This study aimed to evaluate the potential protective effects of KFL on cognitive deficit induced by high-power microwave (HPM) and the underlying mechanism for this neuroprotection. The electron spin resonance technique was employed to evaluate the free radical scavenging activity of KFL in vitro and KFL exhibited scavenging hydroxyl radical activity. KFL at doses of 0.75, 1.5 and 3 g kg-1 and vehicle were administered orally once daily for 14 days to male Wistar rats after being exposed to 30 mW cm-2 HPM for 15 minutes. KFL reversed HPM-induced memory loss and the histopathological changes in hippocampus of rats. In addition, KFL displayed a protective effect against HPM-induced oxidative stress and activated the nuclear factor-E2-related factor 2 (Nrf2) and its target genes in the hippocampus of rats. The Nrf2-antioxidant response element (ARE) signaling pathway may be involved in the neuroprotective effects of KFL against HPM-induced

oxidative stress. In summary, the dietary supplement KFL is a promising natural complex, which ameliorates oxidative stress, with neuroprotective effects against HPM.

(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, EE, BE, WS, SL)

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) Ibitayo AO, Afolabi OB, Akinyemi AJ, Ojiezeh TI, Adekoya KO, Ojewunmi OO. RAPD Profiling, DNA Fragmentation, and Histomorphometric Examination in Brains of Wistar Rats Exposed to Indoor 2.5 Ghz Wi-Fi Devices Radiation. Biomed Res Int. 2017;2017:8653286. (AS, CE, ME)

The advent of Wi-Fi connected high technology devices in executing day-to-day activities is fast evolving especially in developing countries of the world and hence the need to assess its safety among others. The present study was conducted to investigate the injurious effect of radiofrequency emissions from installed Wi-Fi devices in brains of young male rats. Animals were divided into four equal groups; group 1 served as control while groups 2, 3, and 4 were exposed to 2.5 Ghz at intervals of 30, 45, and 60 consecutive days with free access to food and water ad libitum. Alterations in harvested brain tissues were confirmed by histopathological analyses which showed vascular congestion and DNA damage in the brain was assayed using agarose gel electrophoresis. Histomorphometry analyses of their brain tissues showed perivascular congestion and tissue damage as well.

(E) İkinci A, Odacı E, Yıldırım M, Kaya H, Akça M, Hancı H, Aslan A, Sönmez OF, Baş O. The Effects of Prenatal Exposure to a 900 Megahertz Electromagnetic Field on Hippocampus

Morphology and Learning Behavior in Rat Pups. NeuroQuantology. 11(4):582-590, 2013. (AS, BE, ME, CE, DE)

The purpose of this study was to examine the effect on hippocampus morphology and learning behavior in rat pups following prenatal exposure to a 900 megahertz (MHz) electromagnetic field (EMF). Female Sprague Dawley rats weighing 180-250 g were left to mate with males. The following day, pregnant rats identified as such by the vaginal smear test were divided into two groups, control (n=3) and EMF (n=3). No procedures were performed on the control group. The rats in the EMF group were exposed to 900 MHz EMF on days 13 to 21 of pregnancy, for 1 h a day. Female rat pups were removed from their mothers at 22 days old. We then established two newborn rat groups, a 13 member control group and a 10 member EMF group. Radial arm maze and passive avoidance tests were used to measure rat pups' learning and memory performance. All rats were decapitated on the postnatal 32nd day. Routine histological procedures were performed on the brain tissues, and sections were stained with Cresyl fast violet. The radial arm maze (p=0.007) and passive avoidance (p=0.032) tests were administered to both groups under identical conditions, and compromised learning behavior was determined in the EMF group rats. Morphological compromise was also determined in the EMF group sections. Our results show that the application of a 900 MHz EMF in the prenatal period adversely affected female pups' learning behavior and also resulted in histopathological changes appearing in the hippocampus.

E) İkinci A, Mercantepe T, Unal D, Erol HS, Şahin A, Aslan A, Baş O, Erdem H, Sönmez OF, Kaya H, Odacı E. Morphological and antioxidant impairments in the spinal cord of male offspring rats following exposure to a continuous 900MHz electromagnetic field during early and mid-adolescence. 75(Pt B):99-104, 2016. (AS, CE, CH, OX)

The effects of devices emitting electromagnetic field (EMF) on human health have become the subject of intense research among scientists due to the rapid increase in their use. Children and adolescents are particularly attracted to the use of devices emitting EMF, such as mobile phones. The aim of this study was therefore to investigate changes in the spinal cords of male rat pups exposed to the effect of 900MHz EMF. The study began with 24 Sprague-Dawley male rats aged 3 weeks. Three groups containing equal numbers of rats were established-control group (CG), sham group (SG) and EMF group (EMFG). EMFG rats were placed inside an EMF cage every day between postnatal days (PD) 21 and 46 and exposed to the effect of 900MHz EMF for 1h. SG rats were kept in the EMF cage for 1h without being exposed to the effect of EMF. At the end of the study, the spinal cords in the upper thoracic region of all rats were removed. Tissues were collected for biochemistry, light microscopy (LM) and transmission electron microscopic (TEM) examination. Biochemistry results revealed significantly increased malondialdehyde and glutathione levels in EMFG compared to CG and SG, while SG and EMFG catalase and superoxide dismutase levels were significantly higher than those in CG. In EMFG, LM revealed atrophy in the spinal cord, vacuolization, myelin thickening and irregularities in the perikarya. TEM revealed marked loss of myelin sheath integrity and invagination into the axon and broad

vacuoles in axoplasm. The study results show that biochemical alterations and pathological changes may occur in the spinal cords of male rats following exposure to 900MHz EMF for 1h a day on PD 21-46.

(E) Imge EB, Kiliçoğlu B, Devrim E, Cetin R, Durak I. Effects of mobile phone use on brain tissue from the rat and a possible protective role of vitamin C - a preliminary study. Int J Radiat Biol. 86(12):1044-1049, 2010. (AS, CE, CH, OX)

PURPOSE: To evaluate effects of mobile phone use on brain tissue and a possible protective role of vitamin C. **MATERIALS AND METHODS:** Forty female rats were divided into four groups randomly (Control, mobile phone, mobile phone plus vitamin C and, vitamin C alone). The mobile phone group was exposed to a mobile phone signal (900 MHz), the mobile phone plus vitamin C group was exposed to a mobile phone signal (900 MHz) and treated with vitamin C administered orally (per os). The vitamin C group was also treated with vitamin C per os for four weeks. Then, the animals were sacrificed and brain tissues were dissected to be used in the analyses of malondialdehyde (MDA), antioxidant potential (AOP), superoxide dismutase, catalase (CAT), glutathione peroxidase (GSH-Px), xanthine oxidase, adenosine deaminase (ADA) and 5'nucleotidase (5'-NT). **RESULTS:** Mobile phone use caused an inhibition in 5'-NT and CAT activities as compared to the control group. GSH-Px activity and the MDA level were also found to be reduced in the mobile phone group but not significantly. Vitamin C caused a significant increase in the activity of GSH-Px and non-significant increase in the activities of 5'-NT, ADA and CAT enzymes. **CONCLUSION:** Our results suggest that vitamin C may play a protective role against detrimental effects of mobile phone radiation in brain tissue.

(NE) Inomata-Terada S, Okabe S, Arai N, Hanajima R, Terao Y, Frubayashi T, Ugawa Y. Effects of high frequency electromagnetic field (EMF) emitted by mobile phones on the human motor cortex. Bioelectromagnetics. 28(7):553-561, 2007. (HU, EE)

We investigated whether the pulsed high frequency electromagnetic field (EMF) emitted by a mobile phone has short term effects on the human motor cortex. We measured motor evoked potentials (MEPs) elicited by single pulse transcranial magnetic stimulation (TMS), before and after mobile phone exposure (active and sham) in 10 normal volunteers. Three sites were stimulated (motor cortex (CTX), brainstem (BST) and spinal nerve (Sp)). The short interval intracortical inhibition (SICI) of the motor cortex reflecting GABAergic interneuronal function was also studied by paired pulse TMS method. MEPs to single pulse TMS were also recorded in two patients with multiple sclerosis showing temperature dependent neurological symptoms (hot bath effect). Neither MEPs to single pulse TMS nor the SICI was affected by 30 min of EMF exposure from mobile phones or sham exposure. In two MS patients, mobile phone exposure had no effect on any parameters of MEPs even though conduction block occurred at the corticospinal tracts after taking a bath. As far as available methods are concerned, we did not detect any short-term effects of 30 min mobile phone exposure on the human motor cortical output neurons or interneurons even though we can not exclude the possibility that we failed to detect some mild effects due to a small sample size in the present study. This is the first study of MEPs after electromagnetic exposure from a mobile phone in neurological patients.

(NE) Irlenbusch L, Bartsch B, Cooper J, Herget I, Marx B, Raczek J, Thoss F. Influence of a 902.4 MHz GSM signal on the human visual system: investigation of the discrimination threshold. Bioelectromagnetics. 28(8):648-654, 2007. (HU, EE, LI)

The proximity of a mobile phone to the human eye raises the question as to whether radiofrequency (RF) electromagnetic fields (EMF) affect the visual system. A basic characteristic of the human eye is its light sensitivity, making the visual discrimination threshold (VDThr) a suitable parameter for the investigation of potential effects of RF exposure on the eye. The VDThr was measured for 33 subjects under standardized conditions. Each subject took part in two experiments (RF-exposure and sham-exposure experiment) on different days. In each experiment, the VDThr was measured continuously in time intervals of about 10 s for two periods of 30 min, having a break of 5 min in between. The sequence of the two experiments was randomized, and the study was single blinded. During the RF exposure, a GSM signal of 902.4 MHz (pulsed with 217 Hz) was applied to the subjects. The power flux density of the electromagnetic field at the subject location (in the absence of the subject) was 1 W/m(2), and numerical dosimetry calculations determined corresponding maximum local averaged specific absorption rate (SAR) values in the retina of SAR(1 g) = 0.007 W/kg and SAR(10 g) = 0.003 W/kg. No statistically significant differences in the VDThr were found in comparing the data obtained for RF exposure with those for sham exposure.

(E) Jing J, Yuhua Z, Xiao-qian Y, Rongping J, Dong-mei G, Xi C. The influence of microwave radiation from cellular phone on fetal rat brain. Electromagn Biol Med. 31(1):57-66, 2012. (AS, CE, CH, OX, DE)

The increasing use of cellular phones in our society has brought focus on the potential detrimental effects to human health by microwave radiation. The aim of our study was to evaluate the intensity of oxidative stress and the level of neurotransmitters in the brains of fetal rats chronically exposed to cellular phones. The experiment was performed on pregnant rats exposed to different intensities of microwave radiation from cellular phones. Thirty-two pregnant rats were randomly divided into four groups: CG, GL, GM, and GH. CG accepted no microwave radiation, GL group radiated 10 min each time, GM group radiated 30 min, and GH group radiated 60 min. The 3 experimental groups were radiated 3 times a day from the first pregnant day for consecutively 20 days, and on the 21st day, the fetal rats were taken and then the contents of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), malondialdehyde (MDA), noradrenaline (NE), dopamine (DA), and 5-hydroxyindole acetic acid (5-HT) in the brain were assayed. Compared with CG, there were significant differences ($P<0.05$) found in the contents of SOD, GSH-Px, and MDA in GM and GH; the contents of SOD and GSH-Px decreased and the content of MDA increased. The significant content differences of NE and DA were found in fetal rat brains in GL and GH groups, with the GL group increased and the GH group decreased. Through this study, we concluded that receiving a certain period of microwave radiation from cellular phones during pregnancy has certain harm on fetal rat brains.

(E) Jorge-Mora T, Folgueiras MA, Leiro-Vidal JM, Jorge-Barreiro FJ, Ares-Pena FJ, López-Martin E. Exposure to 2.45 GHz Microwave Radiation Provokes Cerebral Changes in Induction of Hsp-90 α/β Heat Shock Protein in Rat. Prog Electromagn Res, 100:351-379, 2010. (AS, CC, CH)

Physical agents such as non-ionizing continuous-wave 2.45 GHz radiation may cause damage that alters cellular homeostasis and may trigger activation of the genes that encode heat shock proteins (HSP). We used Enzyme-Linked ImmunoSorbent Assay (ELISA) and immunohistochemistry to analyze the changes in levels of HSP-90 and its distribution in the brain of Sprague-Dawley rats, ninety minutes and twenty-four hours after acute (30min) continuous exposure to 2.45 GHz radiation in a the Gigahertz Transverse Electromagnetic (GTEM cell). In addition, we studied further indicators of neuronal insult: dark neurons, chromatin condensation and nucleus fragmentation, which were observed under optical conventional or fluorescence microscopy after DAPI staining. The cellular distribution of protein HSP-90 in the brain increased with each corresponding SAR ($0.034 \pm 3.10^{-3,}$ 0.069 ± 5.10^{-3}, 0.27 ± 21.10^{-3} W/kg), in hypothalamic nuclei, limbic cortex and somatosensorial cortex after exposure to the radiation. At twenty-four hours post-irradiation, levels of HSP-90 protein remained high in all hypothalamic nuclei for all SARs, and in the parietal cortex, except the limbic system, HSP-90 levels were lower than in non-irradiated rats, almost half the levels in rats exposed to the highest power radiation. Non-apoptotic cellular nuclei and some dark neurons were found ninety minutes and twenty-four hours after maximal SAR exposure. The results suggest that acute exposure to electromagnetic fields triggered an imbalance in anatomical HSP- 90 levels but the anti-apoptotic mechanism is probably sufficient to compensate the non-ionizing stimulus. Further studies are required to determine the regional effects of chronic electromagnetic pollution on heat shock proteins and their involvement in neurological processes and neuronal damage.

(NE) Joubert V, Leveque P, Cueille M, Bourthoumieu S, Yardin C. No apoptosis is induced in rat cortical neurons exposed to GSM phone fields. Bioelectromagnetics. 28(2):115-121, 2007. (CS, CC)

The aim of this study was to investigate the radiofrequency (RF) electromagnetic fields (EMF) effects on neuronal apoptosis in vitro. Primary cultured neurons from cortices of embryonic Wistar rats were exposed to a 900-MHz global system for mobile communication (GSM) RF field for 24 h in a wire-patch cell. The average-specific absorption rate (SAR) used was 0.25 W/kg. Apoptosis rate was assessed immediately or 24 h after exposure using three methods: (i) DAPI staining; (ii) flow cytometry using double staining with TdT-mediated dUTP nick-end labeling (TUNEL) and propidium iodide (PI); and (iii) measurement of caspase-3 activity by fluorimetry. No statistically significant difference in the apoptosis rate was observed between controls and 24 h GSM-exposed neurons, either 0 h or 24 h post-exposure. All three methods used to assess apoptosis were concordant. These results showed that, under the conditions of experiment used, GSM-exposure does not significantly increase the apoptosis rate in rat primary neuronal cultures. This work is in accordance with other studies performed on cell lines and, to our knowledge, is the first one performed on cultured cortical neurons.

(E) Joubert, V., Bourthoumieu, S., Leveque, P. and Yardin, C. Apoptosis is Induced by Radiofrequency Fields through the Caspase-Independent Mitochondrial Pathway in Cortical Neurons. Radiat. Res. 169, 38-45, 2008. (CS, CC)

In the present study, we investigated whether continuous-wave (CW) radiofrequency (RF) fields induce neuron apoptosis in vitro. Rat primary neuronal cultures were exposed to a CW 900 MHz RF field with a specific absorption rate (SAR) of 2 W/kg for 24 h. During exposure, an increase of 2 degrees C was measured in the medium; control experiments with neurons exposed to 39 degrees C were then performed. Apoptosis was assessed by condensation of nuclei with 4',6-diamino-2-phenylindole (DAPI) staining observed with an epifluorescence microscope and fragmentation of DNA with TdT-mediated dUTP nick-end labeling (TUNEL) analyzed by flow cytometry. A statistically significant difference in the rate of apoptosis was found in the RF-field-exposed neurons compared to the sham-, 37 degrees C- and 39 degrees C-exposed neurons either 0 or 24 h after exposure using both methods. To assess whether the observed apoptosis was caspase-dependent or -independent, assays measuring caspase 3 activity and apoptosis-inducing factor (AIF) labeling were performed. No increase in the caspase 3 activity was found, whereas the percentage of AIF-positive nuclei in RF-field-exposed neurons was increased by three- to sevenfold compared to other conditions. Our results show that, under the experimental conditions used, exposure of primary rat neurons to CW RF fields may induce a caspase-independent pathway to apoptosis that involves AIF.

(E) Jung IS, Kim HJ, Noh R, Kim SC, Kim CW. Effects of extremely low frequency magnetic fields on NGF induced neuronal differentiation of PC12 cells. Bioelectromagnetics. 2014 Aug 26. doi: 10.1002/bem.21861. [Epub ahead of print] (CS, CE, CC, MA)

Extremely low-frequency magnetic fields (ELF-MFs) affect various cellular processes and systems, such as cell proliferation, differentiation and metabolic pathways. The present study investigated ELF-MFs effect on nerve growth factor (NGF) induced neuronal differentiation of PC12 cells using proteomic applications to understand its role in the enhancement of neuronal differentiation. After 50 Hz, 1 mT ELF-MFs 5-day exposure on NGF induced PC12 cells, it was observed to increase neurite length as well as an increase in the number of neurite bearing cells. It was also discovered that there was a decrease in proliferation activity, which is associated with an increase in differentiated cells. Neuronal differentiation related mRNA levels and protein levels were increased in NGF induced PC12 cells. Compared with NGF induced group, ELF-MFs stimulated PC12 cells had different protein expression as measured with two-dimensional electrophoresis (2-DE) gels. Consequently six differentially expressed spots were detected between the 2-DE maps, which were identified by electrospray ionization quadrupole time-of-flight tandem mass spectrometry (ESI-Q-TOF LC/MS/MS) as: peripherin, neurosecretory protein nerve growth factor inducible (VGF8a) precursor, dnaK-type molecular chaperone sp72-ps1 (HSP72-psI), low molecular weight (Mr) phosphotyrosine protein phosphatase isoenzyme AcP1 (LMW-PTP/ACP1), Tubulin alpha-1A (TUBA1A) chain, outcome predictor in acute leukemia 1 homolog (OPA1L). The identification of these proteins provides clues to the mechanism of

ELF-MFs stimulation on NGF induced PC12 cells that occur during neuronal differentiation and may contribute to the development novel treatments for neurodegenerative diseases

(E) Júnior LC, Guimarães ED, Musso CM, Stabler CT, Garcia RM, Mourão-Júnior CA, Andreazzi AE. Behavior and memory evaluation of Wistar rats exposed to 1·8 GHz radiofrequency electromagnetic radiation. Neurol Res. 36:800-803, 2014. (AS, CE, BE)

Background: The development of communication systems has brought great social and economic benefits to society. As mobile phone use has become widespread, concerns have emerged regarding the potential adverse effects of radiofrequency electromagnetic radiation (RF-EMR) used by these devices. Objective: To verify potential effects of mobile phone radiation on the central nervous system (CNS) in an animal model. Methods: Male Wistar rats (60 days old) were exposed to RF-EMR from a Global System for Mobile (GSM) cell phone (1·8 GHz) for 3 days. At the end of the exposure, the following behavioral tests were performed: open field and object recognition. Results: Our results showed that exposed animals did not present anxiety patterns or working memory impairment, but stress behavior actions were observe. Conclusion: Given the results of the present study, we speculate that RF-EMR does not promote CNS impairment, but suggest that it may lead to stressful behavioral patterns.

(NE) Kang KA, Lee HC, Lee JJ, Hong MN, Park MJ, Lee YS, Choi HD, Kim N, Ko YK, Lee JS. Effects of combined radiofrequency radiation exposure on levels of reactive oxygen species in neuronal cells. J Radiat Res. 55:265-276, 2014. (CS, OX, IA)

The objective of this study was to investigate the effects of the combined RF radiation (837 MHz CDMA plus 1950 MHz WCDMA) signal on levels of intracellular reactive oxygen species (ROS) in neuronal cells. Exposure of the combined RF signal was conducted at specific absorption rate values of 2 W/kg of CDMA plus 2 W/kg of WCDMA for 2 h. Co-exposure to combined RF radiation with either H2O2 or menadione was also performed. The experimental exposure groups were incubator control, sham-exposed, combined RF radiation-exposed with or without either H2O2 or menadione groups. The intracellular ROS level was measured by flow cytometry using the fluorescent probe dichlorofluorescein diacetate. Intracellular ROS levels were not consistently affected by combined RF radiation exposure alone in a time-dependent manner in U87, PC12 or SH-SY5Y cells. In neuronal cells exposed to combined RF radiation with either H2O2 or menadione, intracellular ROS levels showed no statically significant alteration compared with exposure to menadione or H2O2 alone. These findings indicate that neither combined RF radiation alone nor combined RF radiation with menadione or H2O2 influences the intracellular ROS level in neuronal cells such as U87, PC12 or SH-SY5Y.

(E) Kaprana AE, Chimona TS, Papadakis CE, Velegrakis SG, Vardiambasis IO, Adamidis G, Velegrakis GA. Auditory brainstem response changes during exposure to GSM-900 radiation: an experimental study. Audiol Neurootol. 16(4):270-276, 2011. (HU, EE)

The objective of the present study was to investigate the possible electrophysiological time-related changes in auditory pathway during mobile phone electromagnetic field exposure. Thirty healthy rabbits were enrolled in an experimental study of exposure to GSM-900 radiation for 60 min and auditory brainstem responses (ABRs) were recorded at regular time-intervals during exposure. The study subjects were radiated via an adjustable power and frequency radio transmitter for GSM-900 mobile phone emission simulation, designed and manufactured according to the needs of the experiment. The mean absolute latency of waves III-V showed a statistically significant delay ($p < 0.05$) after 60, 45 and 15 min of exposure to electromagnetic radiation of 900 MHz, respectively. Interwave latency I-III was found to be prolonged after 60 min of radiation exposure in correspondence to wave III absolute latency delay. Interwave latencies I-V and III-V were found with a statistically significant delay ($p < 0.05$) after 30 min of radiation. No statistically significant delay was found for the same ABR parameters in recordings from the ear contralateral to the radiation source at 60 min radiation exposure compared with baseline ABR. The ABR measurements returned to baseline recordings 24 h after the exposure to electromagnetic radiation of 900 MHz. The prolongation of interval latencies I-V and III-V indicates that exposure to electromagnetic fields emitted by mobile phone can affect the normal electrophysiological activity of the auditory system, and these findings fit the pattern of general responses to a stressor.

(E) Karaca E, Durmaz B, Aktug H, Yildiz T, Guducu C, Irgi M, Koksal MG, Ozkinay F, Gunduz C, Cogulu O. The genotoxic effect of radiofrequency waves on mouse brain. J Neurooncol. 106(1):53-58, 2012. (CS, CH)

Concerns about the health effects of radiofrequency (RF) waves have been raised because of the gradual increase in usage of cell phones, and there are scientific questions and debates about the safety of those instruments in daily life. The aim of this study is to evaluate the genotoxic effects of RF waves in an experimental brain cell culture model. Brain cell cultures of the mice were exposed to 10.715 GHz with specific absorbtion rate (SAR) 0.725 W/kG signals for 6 h in 3 days at 25°C to check for the changes in the micronucleus (MNi) assay and in the expression of 11 proapoptotic and antiapoptotic genes. It was found that MNi rate increased 11-fold and STAT3 expression decreased 7-fold in the cell cultures which were exposed to RF. Cell phones which spread RF may damage DNA and change gene expression in brain cells.

(E) Kerimoğlu G, Hancı H, Baş O, Aslan A, Erol HS, Turgut A, Kaya H, Çankaya S, Sönmez OF, Odacı E. Pernicious effects of long-term, continuous 900-MHz electromagnetic field throughout adolescence on hippocampus morphology, biochemistry and pyramidal neuron numbers in 60-day-old Sprague Dawley male rats. J Chem Neuroanat. 77:169-175, 2016. (AS, CE, ME, OX)

The central nervous system (CNS) begins developing in the intrauterine period, a process that continues until adulthood. Contact with chemical substances, drugs or environmental agents such as electromagnetic field (EMF) during adolescence therefore has the potential to disturb the development of the morphological architecture of components of the CNS (such as the hippocampus). The hippocampus is essential to such diverse functions as memory acquisition and integration and spatial maneuvering. EMF can result in severe damage to both the morphology of the hippocampus and its principal functions during adolescence. Although children and adolescents undergo greater exposure to EMF than adults, the information currently available regarding the effects of exposure to EMF during this period is as yet insufficient. This study investigated the 60-day-old male rat hippocampus following exposure to 900 megahertz (MHz) EMF throughout the adolescent period using stereological, histopathological and biochemical analysis techniques. Eighteen male Sprague Dawley rats aged 21days were assigned into control, sham and EMF groups on a random basis. No procedure was performed on the control group rats. The EMF group (EMFGr) was exposed to a 900-MHz EMF for 1h daily from beginning to end of adolescence. The sham group rats were held in the EMF cage but were not exposed to EMF. All rats were sacrificed at 60days of age. Their brains were extracted and halved. The left hemispheres were set aside for biochemical analyses and the right hemispheres were subjected to stereological and histopathological evaluation. Histopathological examination revealed increased numbers of pyknotic neurons with black or dark blue cytoplasm on EMFGr slides stained with cresyl violet. Stereological analyses revealed fewer pyramidal neurons in EMFGr than in the other two groups. Biochemical analyses showed an increase in malondialdehyde and glutathione levels, but a decrease in catalase levels in EMFGr. Our results indicate that oxidative stress-related morphological damage and pyramidal neuron loss may be observed in the rat hippocampus following exposure to 900-MHz EMF throughout the adolescent period.

(E) Kerimoğlu G, Aslan A, Baş O, Çolakoğlu S, Odacı E. Adverse effects in lumbar spinal cord morphology and tissue biochemistry in Sprague Dawley male rats following exposure to a continuous 1-h a day 900-MHz electromagnetic field throughout adolescence. J Chem Neuroanat. 78:125-130, 2016. (AS, CE, ME, OX)

Cell phones, an indispensable element of daily life, are today used at almost addictive levels by adolescents. Adolescents are therefore becoming increasingly exposed to the effect of the electromagnetic field (EMF) emitted by cell phones. The purpose of this study was to investigate the effect of exposure to a 900-MHz EMF throughout adolescence on the lumbar spinal cord using histopathological, immunohistochemical and biochemical techniques. Twenty-four Sprague Dawley (28.3-43.9g) aged 21days were included in the study. These were divided equally into three groups - control (CG), sham (SG) and electromagnetic (ELMAG). No procedure was performed on the CG rats until the end of the study. SG and ELMAG rats were kept inside an EMF cage (EMFC) for 1h a day every day at the same time between postnatal days 22 and 60. During this time, ELMAG rats were exposed to the effect of a 900-MHz EMF, while the SG rats were kept in the EMFC without being exposed to EMF. At the end of the study, the lumbar regions of the spinal cords of all rats in all groups were extracted. Half of each extracted tissue

was stored at -80°C for biochemical analysis, while the other half was used for histopathological and immunohistochemical analyses. In terms of histopathology, a lumbar spinal cord with normal morphology was observed in the other groups, while morphological irregularity in gray matter, increased vacuolization and infiltration of white matter into gray matter were pronounced in the ELMAG rats. The cytoplasm of some neurons in the gray matter was shrunken and stained dark, and vacuoles were observed in the cytoplasms. The apoptotic index of glia cells and neurons were significantly higher in ELMAG compared to the other groups. Biochemical analysis revealed a significantly increased MDA value in ELMAG compared to CG, while SOD and GSH levels decreased significantly. In conclusion, our study results suggest that continuous exposure to a 900-MHz EMF for 1h a day through all stages of adolescence can result in impairments at both morphological and biochemical levels in the lumbar region spinal cords of Sprague Dawley rats.

(E) Kesari KK, Kumar S, Behari J. 900-MHz microwave radiation promotes oxidation in rat brain. Electromagn Biol Med. 30(4):219-234, 2011. (AS, CE, CH, OX)

Recently, there have been several reports referring to detrimental effects due to radio frequency electromagnetic fields (RF-EMF) exposure. Special attention was given to investigate the effect of mobile phone exposure on the rat brain. Since the integrative mechanism of the entire body lies in the brain, it is suggestive to analyze its biochemical aspects. For this, 35-day old Wistar rats were exposed to a mobile phone for 2 h per day for a duration of 45 days where specific absorption rate (SAR) was 0.9 W/Kg. Animals were divided in two groups: sham exposed (n = 6) and exposed group (n = 6). Our observations indicate a significant decrease ($P < 0.05$) in the level of glutathione peroxidase, superoxide dismutase, and an increase in catalase activity. Moreover, protein kinase shows a significant decrease in exposed group ($P < 0.05$) of hippocampus and whole brain. Also, a significant decrease ($P < 0.05$) in the level of pineal melatonin and a significant increase ($P < 0.05$) in creatine kinase and caspase 3 was observed in exposed group of whole brain as compared with sham exposed. Finally, a significant increase in the level of ROS (reactive oxygen species) ($P < 0.05$) was also recorded. The study concludes that a reduction or an increase in antioxidative enzyme activities, protein kinase C, melatonin, caspase 3, and creatine kinase are related to overproduction of reactive oxygen species (ROS) in animals under mobile phone radiation exposure. Our findings on these biomarkers are clear indications of possible health implications.

(E) Kesari KK, Meena R, Nirala J, Kumar J, Verma HN. Effect of 3G cell phone exposure with computer controlled 2-D stepper motor on non-thermal activation of the hsp27/p38MAPK stress pathway in rat brain. Cell Biochem Biophys. 68(2):347-358, 2014. (AS, CE, CH)

Cell phone radiation exposure and its biological interaction is the present concern of debate. Present study aimed to investigate the effect of 3G cell phone exposure with computer controlled 2-D stepper motor on 45-day-old male Wistar rat brain. Animals were exposed for 2 h a day for 60 days by using mobile phone with angular movement up to zero to 30°. The variation of the motor is restricted to 90° with respect to the horizontal plane, moving at a pre-determined rate of 2° per minute. Immediately after 60 days of exposure, animals were

scarified and numbers of parameters (DNA double-strand break, micronuclei, caspase 3, apoptosis, DNA fragmentation, expression of stress-responsive genes) were performed. Result shows that microwave radiation emitted from 3G mobile phone significantly induced DNA strand breaks in brain. Meanwhile a significant increase in micronuclei, caspase 3 and apoptosis were also observed in exposed group ($P < 0.05$). Western blotting result shows that 3G mobile phone exposure causes a transient increase in phosphorylation of hsp27, hsp70, and p38 mitogen-activated protein kinase (p38MAPK), which leads to mitochondrial dysfunction-mediated cytochrome c release and subsequent activation of caspases, involved in the process of radiation-induced apoptotic cell death. Study shows that the oxidative stress is the main factor which activates a variety of cellular signal transduction pathways, among them the hsp27/p38MAPK is the pathway of principle stress response. Results conclude that 3G mobile phone radiations affect the brain function and cause several neurological disorders.

(E) Khullar S1, Sood A2, Sood S3. Auditory Brainstem Responses and EMFs Generated by Mobile Phones. Indian J Otolaryngol Head Neck Surg. 65(Suppl 3):645-649, 2013. (HU, EE)

There has been a manifold increase in the number of mobile phone users throughout the world with the current number of users exceeding 2 billion. However this advancement in technology like many others is accompanied by a progressive increase in the frequency and intensity of electromagnetic waves without consideration of the health consequences. The aim of our study was to advance our understanding of the potential adverse effects of GSM mobile phones on auditory brainstem responses (ABRs). 60 subjects were selected for the study and divided into three groups of 20 each based on their usage of mobile phones. Their ABRs were recorded and analysed for latency of waves I-V as well as interpeak latencies I-III, I-V and III-V (in ms). Results revealed no significant difference in the ABR parameters between group A (control group) and group B (subjects using mobile phones for maximum 30 min/day for 5 years). However the latency of waves was significantly prolonged in group C (subjects using mobile phones for 10 years for a maximum of 30 min/day) as compared to the control group. Based on our findings we concluded that long term exposure to mobile phones may affect conduction in the peripheral portion of the auditory pathway. However more research needs to be done to study the long term effects of mobile phones particularly of newer technologies like smart phones and 3G.

(NE) Kim HS, An YS, Paik MJ, Lee YS, Choi HD, Kim BC, Pack JK, Kim N, Ahn YH. The effects of exposure to 915 MHz radiofrequency identification on cerebral glucose metabolism in rat: A [F-18] FDG micro-PET study. Int J Radiat Biol. 2013 May 7. [Epub ahead of print] (AS, CE, CC, CH)

Purpose: We investigated the effect of whole-body exposure to 915-MHz radiofrequency identification (RFID) on rat cortical glucose metabolism by using ^{18}F-deoxyglucose positron emission tomography (FDG-PET). Materials and methods: Male Sprague-Dawley rats were divided into three groups: Cage-control, sham-exposed and RFID-exposed groups. Rats were exposed to the 915-MHz RFID for 8 h daily, 5 days per week, for 2 or 16 weeks. The whole-body

average specific absorption rate (SAR) was 4 W/kg for the field of the 915 MHz RFID signal. FDG-PET images were obtained the day after RFID exposure, using micro-PET with a FDG tracer. With a Xeleris functional imaging workstation, absolute values in regions of interest (ROI) in the frontal, temporal and parietal cortexes and cerebellum were measured. Cortical ROI values were normalized to the cerebellar value and compared. Results: The data showed that the relative cerebral glucose metabolic rate was unchanged in the frontal, temporal and parietal cortexes of the 915 MHz RFID-exposed rats, compared with rats in cage-control and sham-exposed groups. Conclusion: Our results suggest that 915 MHz RFID radiation exposure did not cause a significant long lasting effect on glucose metabolism in the rat brain.

(NE) Kim HS, Kim YJ, Lee YH, Lee YS, Choi HD, Pack JK, Kim N, Ahn YH. Effect of whole-body exposure to the 848.5-MHz code division multiple access (CDMA) electromagnetic field on adult neurogenesis in the young, healthy rat brain. Int J Radiat Biol. 2014 Dec 15:1-15. [Epub ahead of print] (AS, CE, CC)

Introduction: Whether exposure to the 848.5-MHz code division multiple access (CDMA) signal affects adult neurogenesis is unclear. Materials and methods: An animal experiment was performed with a reverberation chamber designed as a whole-body CDMA exposure system. Male Sprague-Dawley rats were assigned to three groups (n = 6 per group): cage-control, sham-exposed, and CDMA-exposed groups. Rats in the CDMA-exposed group were exposed to the CDMA signal at a 2 W/kg whole-body specific absorption rate (SAR) for 1 or 8 h daily, 5 days per week, for 2 weeks. Rats received a single intraperitoneal injection of Bromodeoxyuridine (BrdU) to label proliferative cells daily for the last five consecutive days of CDMA signal exposure. An unbiased stereological method was used to estimate the number of $BrdU^+$ cells in the subventricular zone (SVZ) and dentate gyrus (DG). Results: We found no significant changes in the number of $BrdU^+$ cells in the SVZ or DG in the CDMA-exposed rats, compared with rats in the cage-control and sham-exposed groups ($p > 0.05$). Conclusion: Our results suggest that exposure to the CDMA signal does not affect neurogenesis in the adult rat brain, at least under our experimental conditions.

(E) Kim JH, Yu DH, Huh YH, Lee EH, Kim HG, Kim HR. Long-term exposure to 835 MHz RF-EMF induces hyperactivity, autophagy and demyelination in the cortical neurons of mice. Sci Rep. 7:41129, 2017. (AS, CE, BE, CC)

Radiofrequency electromagnetic field (RF-EMF) is used globally in conjunction with mobile communications. There are public concerns of the perceived deleterious biological consequences of RF-EMF exposure. This study assessed neuronal effects of RF-EMF on the cerebral cortex of the mouse brain as a proxy for cranial exposure during mobile phone use. C57BL/6 mice were exposed to 835 MHz RF-EMF at a specific absorption rate (SAR) of 4.0 W/kg for 5 hours/day during 12 weeks. The aim was to examine activation of autophagy pathway in the cerebral cortex, a brain region that is located relatively externally. Induction of autophagy genes and production of proteins including LC3B-II and Beclin1 were increased and accumulation of autolysosome was observed in neuronal cell bodies. However, proapoptotic factor Bax was down-regulted in the cerebral cortex. Importantly, we found that RF-EMF exposure led to myelin sheath damage and mice displayed hyperactivity-like behaviour. The data suggest that

autophagy may act as a protective pathway for the neuronal cell bodies in the cerebral cortex during radiofrequency exposure. The observations that neuronal cell bodies remained structurally stable but demyelination was induced in cortical neurons following prolonged RF-EMF suggests a potential cause of neurological or neurobehavioural disorders.

(E) Kim JH, Yu DH, Kim HJ, Huh YH, Cho SW, Lee JK, Kim HG, Kim HR. Exposure to 835 MHz radiofrequency electromagnetic field induces autophagy in hippocampus but not in brain stem of mice. Toxicol Ind Health. 2017 Jan 1:748233717740066. doi: 10.1177/0748233717740066. [Epub ahead of print] (AS, CE, ME)

The exploding popularity of mobile phones and their close proximity to the brain when in use has raised public concern regarding possible adverse effects from exposure to radiofrequency electromagnetic fields (RF-EMF) on the central nervous system. Numerous studies have suggested that RF-EMF emitted by mobile phones can influence neuronal functions in the brain. Currently, there is still very limited information on what biological mechanisms influence neuronal cells of the brain. In the present study, we explored whether autophagy is triggered in the hippocampus or brain stem after RF-EMF exposure. C57BL/6 mice were exposed to 835 MHz RF-EMF with specific absorption rates (SAR) of 4.0 W/kg for 12 weeks; afterward, the hippocampus and brain stem of mice were dissected and analyzed. Quantitative real-time polymerase chain reaction (qRT-PCR) analysis demonstrated that several autophagic genes, which play key roles in autophagy regulation, were significantly upregulated only in the hippocampus and not in the brain stem. Expression levels of LC3B-II protein and p62, crucial autophagic regulatory proteins, were significantly changed only in the hippocampus. In parallel, transmission electron microscopy (TEM) revealed an increase in the number of autophagosomes and autolysosomes in the hippocampal neurons of RF-EMF-exposed mice. The present study revealed that autophagy was induced in the hippocampus, not in the brain stem, in 835 MHz RF-EMF with an SAR of 4.0 W/kg for 12 weeks. These results could suggest that among the various adaptation processes to the RF-EMF exposure environment, autophagic degradation is one possible mechanism in specific brain regions.

(E) Kim JY, Kim HJ, Kim N, Kwon JH, Park MJ. Effects of radiofrequency field exposure on glutamate-induced oxidative stress in mouse hippocampal HT22 cells. Int J Radiat Biol. 93:249-256, 2017. (CS, CC, OX, IA)

PURPOSE: To define the impact of radiofrequency (RF) under in vitro experimental Alzheimer's disease conditions, we investigated the effect of RF radiation on glutamate-induced oxidative stress in mouse hippocampal neuronal HT22 cells. MATERIALS AND METHODS: Cell survival rate was measured by MTT and trypan blue exclusion assays. Cell cycle distribution, cell death, and ROS production were analyzed using flow cytometry. Expression of proteins was analyzed by Western blot. RESULTS: RF exposure alone had a marginal impact on cell proliferation, however significantly enhanced glutamate-induced cytotoxicity in HT22 cells. Glutamate augmented the subG1 fraction of cell cycle, annexin/propidium iodide positive cell population, and expression of cleaved poly (ADP ribose) polymerase, which were further increased by RF exposure. Glutamate induced reactive oxygen species (ROS) generation and RF exposure

further upregulated it. N-acetylcysteine (NAC) treatment completely abrogated glutamate- and RF-induced ROS production followed by cell death and restored cell proliferation in HT22 cells. Finally, glutamate phosphorylated c-Jun N-terminal kinase (JNK) and RF increased this event further. Treatment with NAC and inhibitor of JNK decreased JNK phosphorylation and restored cell proliferation, respectively. CONCLUSIONS: Our results demonstrate that RF exposure enhanced glutamate-induced cytotoxicity by further increase of ROS production in HT22 cells.

(E) Kim JH, Kim HJ, Yu DH, Kweon HS, Huh YH, Kim HR. Changes in numbers and size of synaptic vesicles of cortical neurons induced by exposure to 835 MHz radiofrequency-electromagnetic field. PLoS One. 12(10):e0186416, 2017. (AS, CE, ME, CH)

We studied the effects of radiofrequency electromagnetic fields (RF-EMFs) exposure on neuronal functions of mice. Particularly, we focused on RF-EMF effects on synaptic vesicles (SVs), which store neurotransmitters at axon terminals or synaptic boutons. C57 BL/6 mice were exposed to 835 MHz RF-EMF (4.0 W/kg SAR, for 5 h daily) and alterations in SVs at presynaptic terminals in the cerebral cortex were determined. Ultrastructure of randomly selected cortical neurons was observed using typical electron microscopy and bio-high voltage electron microscopy (Bio-HVEM) methods, which enable the estimation of the numbers and size of SVs. The density of the SVs (number /10 μm2 or 40 μm3) was significantly decreased in the presynaptic boutons of cortical neurons after RF-EMF exposure. Furthermore, qPCR and immunoblotting analyses revealed that the expression of synapsins I/II (Syns I/II) genes and proteins were significantly decreased in the cortical neurons of RF-EMF exposed mice. The present study suggested that alteration of SVs and Syn levels may result in alterations of neurotransmitters in the cerebral cortex following RF-EMF exposure.

(NE) Kim TH, Huang TQ, Jang JJ, Kim MH, Kim HJ, Lee JS, Pack JK, Seo JS, Park WY. Local exposure of 849 MHz and 1763 MHz radiofrequency radiation to mouse heads does not induce cell death or cell proliferation in brain. Exp Mol Med. 40(3):294-303, 2008. (AS, CE, CC)
Erratum in: Exp Mol Med. 2008 Aug 31;40(4):477. Kim, Tae-Hyoung [corrected to Kim, Tae-Hyung].

Even though there is no direct evidence to prove the cellular and molecular changes induced by radiofrequency (RF) radiation itself, we cannot completely exclude the possibility of any biological effect of mobile phone frequency radiation. We established a carousel-type exposure chamber for 849 MHz or 1763 MHz of mobile phone RF radiation to expose RF to the heads of C57BL mice. In this chamber, animals were irradiated intermittently at 7.8 W/kg for a maximum of 12 months. During this period, the body weights of 3 groups-sham, 849 MHz RF, and 1763 MHz RF-did not show any differences between groups. The brain tissues were obtained from 3 groups at 6 months and 12 months to examine the differences in histology and cell proliferation between control and RF exposure groups, but we could not find any change upon RF radiation. Likewise, we could not find changes in the expression and distribution of NeuN and GFAP in hippocampus and cerebellum, or in cell death by TUNEL assay in RF exposure groups. From these data, we conclude that the chronic exposure to 849 MHz and 1763 MHz RF radiation at a

7.8 W/kg specific absorption rate (SAR) could not induce cellular alterations such as proliferation, death, and reactive gliosis.

(NE) Kleinlogel H, Dierks T, Koenig T, Lehmann H, Minder A, Berz R. Effects of weak mobile phone - electromagnetic fields (GSM, UMTS) on well-being and resting EEG. Bioelectromagnetics. 29(6):479-487, 2008a. (HU, BE, EE)

Modern mobile phones emit electromagnetic fields (EMFs) ranging from 900 to 2000 MHz which are suggested to have an influence on well-being, attention and neurological parameters in mobile phone users. To date most studies have investigated Global System for Mobile Communications (GSM)-EMF and only very few studies were concerned with Universal Mobile Telecommunications System (UMTS)-EMF. Consequently, we tested the effects of both types of EMF, 1950 MHz UMTS (SAR 0.1 and 1 W/kg) and pulsed 900 MHz GSM (1 W/kg), *on* well-being and vigilance-controlled resting electroencephalogram (eyes closed) in 15 healthy, right-handed subjects. A double-blind, randomised, crossover application of the test procedure was used. Neither the UMTS- nor the GSM-EMF produced any significant changes in the measured parameters compared to sham exposure. The results do not give any evidence for a deleterious effect of the EMF on normal healthy mobile phone users.

(NE) Kleinlogel H, Dierks T, Koenig T, Lehmann H, Minder A, Berz R. Effects of weak mobile phone - electromagnetic fields (GSM, UMTS) on event related potentials and cognitive functions. Bioelectromagnetics. 29(6):488-497, 2008b. (HU, EE, BE)

Modern mobile phones emit electromagnetic fields (EMF) ranging from 900 to 2000 MHz which are suggested to have an influence on well-being, attention and neurological parameters in mobile phone users. Until now most studies have investigated Global System for Mobile Communications (GSM)-EMF and only very few studies have focused on Universal Mobile Telecommunications System (UMTS)-EMF. Therefore, we tested the effects of both types of unilaterally presented EMF, 1950 UMTS (0.1 and 1 W/kg) and pulsed 900 MHz GSM (1 W/kg), on visually evoked occipital P100, the P300 of a continuous performance test, auditory evoked central N100 and the P300 during an oddball task as well as on the respective behavioral parameters, reaction time and false reactions, in 15 healthy, right handed subjects. A double-blind, randomized, crossover application of the test procedure was used. Neither the UMTS- nor the GSM-EMF produced any significant changes in the measured parameters compared to sham exposure. The results do not give any evidence for a deleterious effect of the EMF on normal healthy mobile phone users.

(NE) Klose M, Grote K, Spathmann O, Streckert J, Clemens M, Hansen VW, Lerchl A. Effects of early-onset radiofrequency electromagnetic field exposure (GSM 900 MHz) on behavior and memory in rats. Radiat Res. 182(4):435-447, 2014. (AS, CE, BE)

Female Wistar rats, from an age of 14 days to 19 months, were exposed in the head region for 2 h per day, 5 days per week, to a GSM-modulated 900 MHz radiofrequency electromagnetic field (RF-EMF). The average specific absorption rates (SAR) in the brain were 0 (sham), 0.7, 2.5 and

10 W/kg. To ensure a primary exposure of the head region, rats were fixed in restraining tubes of different sizes according to their increasing body weight. During the experiment, a set of 4 behavioral and learning tests (rotarod, Morris water maze, 8-arm radial maze, open field) were performed 3 times in juvenile, adult and presenile rats. In these tests, no profound differences could be identified between the groups. Only presenile rats of the cage control group showed a lower activity in two of these tests compared to the other groups presumably due to the lack of daily handling. The rotarod data revealed on some testing days significantly longer holding times for the sham-exposed rat vs. the exposed rat, but these findings were not consistent. During the first year, body weights of sham-exposed and exposed rats were not different from those of the cage controls, and thereafter only marginally lower, so that the effect of stress as confounder was probably negligible. The results of this study do not indicate harmful effects of long-term RF-EMF exposure even when begun at an early age on subsequent development, learning skills and behavior in rats, even at relatively high SAR values.

(E) Köktürk S, Yardimoglu M, Celikozlu SD, Dolanbay EG, Cimbiz A. Effect of Lycopersicon esculentum extract on apoptosis in the rat cerebellum, following prenatal and postnatal exposure to an electromagnetic field. Exp Ther Med. 6(1):52-56, 2013. (AS, CE, DE, CC)

The expansion of mobile phone technology has raised concerns regarding the effect of 900-MHz electromagnetic field (EMF) exposure on the central nervous system. At present, the developing human brain is regularly exposed to mobile telephones, pre- and postnatally. Several studies have demonstrated the acute effects of EMF exposure during pre- or postnatal periods; however, the chronic effects of EMF exposure are less understood. Thus, the aim of the present study was to determine the chronic effects of EMF on the pre- and postnatal rat cerebellum. The control group was maintained in the same conditions as the experimental groups, without the exposure to EMF. In the EMF1 group, the rats were exposed to EMF during pre- and postnatal periods (until postnatal day 80). In the EMF2 group, the rats were also exposed to EMF pre- and postnatally; in addition, however, they were provided with a daily oral supplementation of *Lycopersicon esculentum* extract (~2 g/kg). The number of caspase-3-labeled Purkinje neurons and granule cells present in the rats in the control and experimental groups were then counted. The neurodegenerative changes were studied using cresyl violet staining, and these changes were evaluated. In comparison with the control animals, the EMF1 group demonstrated a significant increase in the number of caspase-3-labeled Purkinje neurons and granule cells present in the cerebellum ($P<0.001$). However, in comparison with the EMF1 group, the EMF2 group exhibited significantly fewer caspase-3-labeled Purkinje neurons and granule cells in the cerebellum. In the EMF1 group, the Purkinje neurons were revealed to have undergone dark neuron degenerative changes. However, the presence of dark Purkinje neurons was reduced in the EMF2 group, compared with the EMF1 group. The results indicated that apoptosis and neurodegeneration in rats exposed to EMF during pre- and postnatal periods may be reduced with *Lycopersicon esculentum* extract therapy.

(NE) Krause CM, Pesonen M, Haarala Björnberg C, Hämäläinen H. Effects of pulsed and continuous wave 902 MHz mobile phone exposure on brain oscillatory activity during cognitive processing. Bioelectromagnetics. 28(4):296-308, 2007. (HU, EE)

The aim of the current double-blind studies was to partially replicate the studies by Krause et al. [2000ab, 2004] and to further investigate the possible effects of electromagnetic fields (EMF) emitted by mobile phones (MP) on the event-related desynchronisation/synchronisation (ERD/ERS) EEG (electroencephalogram) responses during cognitive processing. Two groups, both consisting of 36 male participants, were recruited. One group performed an auditory memory task and the other performed a visual working memory task in six exposure conditions: SHAM (no EMF), CW (continuous wave EMF) and PM (pulse modulated EMF) during both left- and right-side exposure, while the EEG was recorded. In line with our previous studies, we observed that the exposure to EMF had modest effects on brain oscillatory responses in the alpha frequency range (approximately 8-12 Hz) and had no effects on the behavioural measures. The effects on the EEG were, however, varying, unsystematic and inconsistent with previous reports. We conclude that the effects of EMF on brain oscillatory responses may be subtle, variable and difficult to replicate for unknown reasons.

(E) Kumar RS, Sareesh NN, Nayak S, Mailankot M. Hypoactivity of Wistar rats exposed to mobile phone on elevated plus maze. Indian J Physiol Pharmacol. 53(3):283-286, 2009. (AS, BE)

No abstract available. From discussion section: “In conclusion, our preliminary results indicate mobile phone exposure induced behavioral changes in rats, expressed as deficit in open arm exploration on elevated plus-maze.”

(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. 2017 Dec 4;12(12):e0188880. (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.

(E) Kumlin T, Iivonen H, Miettinen P, Juvonen A, van Groen T, Puranen L, Pitkäaho R, Juutilainen J, Tanila H. Mobile phone radiation and the developing brain: behavioral and morphological effects in juvenile rats. Radiat Res. 168(4):471-479, 2007. (AS, CE, ME, BE)

The increasing use of mobile phones by children and teenagers has raised concerns about their safety. Addressing such concerns is difficult, because no data are available on possible effects from long-term exposure to radiofrequency (RF) fields during the development of the nervous system. Possible morphological and functional changes were evaluated in the central nervous system of young male Wistar rats exposed to 900 MHz mobile phone signal for 2 h/day on 5 days/week. After 5 weeks of exposure at whole-body average specific energy absorption rates of 0.3 or 3.0 W/kg or sham exposure, six rats per group were examined histologically, and the remaining 18 rats per group were subjected to behavioral tests. No degenerative changes, dying neurons, or effects on the leakage of the blood-brain barrier were detected. No group differences were observed in the open-field test, plus maze test or acoustic startle response tests. In the water maze test, however, significantly improved learning ($P = 0.012$) and memory ($P = 0.01$) were detected in rats exposed to RF fields. The results do not indicate a serious threat to the developing brain from mobile phone radiation at intensities relevant to human exposure. However, the interesting finding of improved learning and memory warrants further studies.

(NE) Kwon MS, Kujala T, Huotilainen M, Shestakova A, Näätänen R, Hämäläinen H. Preattentive auditory information processing under exposure to the 902 MHz GSM mobile phone electromagnetic field: a mismatch negativity (MMN) study. Bioelectromagnetics. 30(3):241-248, 2009. (HU, EE)

Previous studies on the effects of the mobile phone electromagnetic field (EMF) on various event-related potential (ERP) components have yielded inconsistent and even contradictory results, and often failed in replication. The mismatch negativity (MMN) is an auditory ERP component elicited by infrequent (deviant) stimuli differing in some physical features from the repetitive frequent (standard) stimuli in a sound sequence. The MMN provides a sensitive measure for cortical auditory stimulus feature discrimination, regardless of attention and other contaminating factors. In this study, MMN responses to duration, intensity, frequency, and gap changes were recorded in healthy young adults (n = 17), using a multifeature paradigm including several types of auditory change in the same stimulus sequence, while a GSM mobile phone was placed on either ear with the EMF (902 MHz pulsed at 217 Hz; SAR(1g) = 1.14 W/kg, SAR(10g) = 0.82 W/kg, peak value = 1.21 W/kg, measured with an SAM phantom) on or off. An MMN was elicited by all deviant types, while its amplitude and latency showed no significant differences due to EMF exposure for any deviant types. In the present study, we found no conclusive evidence that acute exposure to GSM mobile phone EMF affects cortical auditory change detection processing reflected by the MMN.

(NE) Kwon MS, Jääskeläinen SK, Toivo T, Hämäläinen H. No effects of mobile phone electromagnetic field on auditory brainstem response. Bioelectromagnetics. 31(1):48-55, 2010a. (HU, EE)

The present study investigated the possible effects of the electromagnetic field (EMF) emitted by an ordinary GSM mobile phone (902.4 MHz pulsed at 217 Hz) on brainstem auditory processing. Auditory brainstem responses (ABR) were recorded in 17 healthy young adults, without a mobile phone at baseline, and then with a mobile phone on the ear under EMF-off and EMF-on conditions. The amplitudes, latencies, and interwave intervals of the main ABR components (waves I, III, V) were compared among the three conditions. ABR waveforms showed no significant differences due to exposure, suggesting that short-term exposure to mobile phone EMF did not affect the transmission of sensory stimuli from the cochlea up to the midbrain along the auditory nerve and brainstem auditory pathways.

(NE) Kwon MS, Huotilainen M, Shestakova A, Kujala T, Näätänen R, Hämäläinen H. No effects of mobile phone use on cortical auditory change-detection in children: an ERP study. Bioelectromagnetics. 31(3):191-199, 2010b. (HU, EE)

We investigated the effect of mobile phone use on the auditory sensory memory in children. Auditory event-related potentials (ERPs), P1, N2, mismatch negativity (MMN), and P3a, were recorded from 17 children, aged 11-12 years, in the recently developed multi-feature paradigm. This paradigm allows one to determine the neural change-detection profile consisting of several different types of acoustic changes. During the recording, an ordinary GSM (Global System for Mobile Communications) mobile phone emitting 902 MHz (pulsed at 217 Hz) electromagnetic field (EMF) was placed on the ear, over the left or right temporal area (SAR(1g) = 1.14 W/kg, SAR(10g) = 0.82 W/kg, peak value = 1.21 W/kg). The EMF was either on or off in a single-blind manner. We found that a short exposure (two 6 min blocks for each side) to mobile phone EMF has no statistically significant effects on the neural change-detection profile measured with the MMN. Furthermore, the multi-feature paradigm was shown to be well suited for studies of perception accuracy and sensory memory in children. However, it should be noted that the present study only had sufficient statistical power to detect a large effect size.

(NE) Kwon MS, Vorobyev V, Kännälä S, Laine M, Rinne JO, Toivonen T, Johansson J, Teräs M, Joutsa J, Tuominen L, Lindholm H, Alanko T, Hämäläinen H. No effects of short-term GSM mobile phone radiation on cerebral blood flow measured using positron emission tomography. Bioelectromagnetics. 33(3):247-256, 2012. (HU, PE)

The present study investigated the effects of 902.4 MHz global system for mobile communications (GSM) mobile phone radiation on cerebral blood flow using positron emission tomography (PET) with the (15) O-water tracer. Fifteen young, healthy, right-handed male subjects were exposed to phone radiation from three different locations (left ear, right ear, forehead) and to sham exposure to test for possible exposure effects on brain regions close to the exposure source. Whole-brain [^{15}O]H_2O-PET images were acquired 12 times, 3 for each condition, in a counterbalanced order. Subjects were exposed for 5 min in each scan while

performing a simple visual vigilance task. Temperature was also measured in the head region (forehead, eyes, cheeks, ear canals) during exposure. The exposure induced a slight temperature rise in the ear canals but did not affect brain hemodynamics and task performance. The results provided no evidence for acute effects of short-term mobile phone radiation on cerebral blood flow.

(E) Kwon MS, Vorobyev V, Kännälä S, Laine M, Rinne JO, Toivonen T, Johansson J, Teräs M, Lindholm H, Alanko T, Hämäläinen H. GSM mobile phone radiation suppresses brain glucose metabolism. J Cereb Blood Flow Metab. 31(12):2293-2301, 2011. (HU, PE)

We investigated the effects of mobile phone radiation on cerebral glucose metabolism using high-resolution positron emission tomography (PET) with the (18)F-deoxyglucose (FDG) tracer. A long half-life (109 minutes) of the (18)F isotope allowed a long, natural exposure condition outside the PET scanner. Thirteen young right-handed male subjects were exposed to a pulse-modulated 902.4 MHz Global System for Mobile Communications signal for 33 minutes, while performing a simple visual vigilance task. Temperature was also measured in the head region (forehead, eyes, cheeks, ear canals) during exposure. (18)F-deoxyglucose PET images acquired after the exposure showed that relative cerebral metabolic rate of glucose was significantly reduced in the temporoparietal junction and anterior temporal lobe of the right hemisphere ipsilateral to the exposure. Temperature rise was also observed on the exposed side of the head, but the magnitude was very small. The exposure did not affect task performance (reaction time, error rate). Our results show that short-term mobile phone exposure can locally suppress brain energy metabolism in humans.

(E) Lee D, Lee J, Lee I. Cell Phone Generated Radio Frequency Electromagnetic Field Effects on the Locomotor Behaviors of the Fishes Poecilia reticulata and Danio rerio. Int J Radiat Biol. 2015 Jun 15:1-20. [Epub ahead of print] (AS, BE)

PURPOSE: The locomotor behavior of small fish was characterized under a cell phone generated radio frequency electromagnetic field (RF EMF). MATERIALS AND METHODS: The trajectory of movement of 10 pairs of poecilia reticulata and 15 pairs of danio rerio in a fish tank was recorded and tracked under the presence of a cell phone generated RF EMF. The measures were based on spatial and temporal distributions. A time-series trajectory was utilized to emphasis the dynamic nature of locomotor behavior. Fish movement was recorded in real-time. Their spatial, velocity, turning angle and sinuosity distribution were analyzed in terms of F(v,x), P[n(x,t)], P(v), F (Θ) and F(s), respectively. In addition, potential temperature elevation caused by a cellular phone was also examined. RESULTS: We demonstrated that a cellular phone induced temperature elevation was not relevant, and that our measurements reflected RF EMF-induced effects on the locomotor behavior of poecilia reticulata and danio rerio. Fish locomotion was observed under normal conditions, in the visual presence of a cell phone, after feeding, and under starvation. Fish locomotor behavior was random both in normal conditions and in the presence of an off-signaled cell phone. However, there were significant changes in

the locomotion of the fish after feeding under the RF EMF. CONCLUSIONS: The locomotion of the fed fish was affected in terms of changes in population and velocity distributions under the presence of the RF EMF emitted by the cell phone. There was, however, no significant difference in angular distribution.

(E) Lee KS, Choi JS, Hong SY, Son TH, Yu K. Mobile phone electromagnetic radiation activates MAPK signaling and regulates viability in Drosophila. Bioelectromagnetics. 29(5):371-379, 2008. (AS, CC)

Mobile phones are widely used in the modern world. However, biological effects of electromagnetic radiation produced by mobile phones are largely unknown. In this report, we show biological effects of the mobile phone 835 MHz electromagnetic field (EMF) in the Drosophila model system. When flies were exposed to the specific absorption rate (SAR) 1.6 W/kg, which is the proposed exposure limit by the American National Standards Institute (ANSI), more than 90% of the flies were viable even after the 30 h exposure. However, in the SAR 4.0 W/kg strong EMF exposure, viability dropped from the 12 h exposure. These EMF exposures triggered stress response and increased the production of reactive oxygen species. The EMF exposures also activated extracellular signal regulated kinase (ERK) and c-Jun N-terminal kinase (JNK) signaling, but not p38 kinase signaling. Interestingly, SAR 1.6 W/kg activated mainly ERK signaling and expression of an anti-apoptotic gene, whereas SAR 4.0 W/kg strongly activated JNK signaling and expression of apoptotic genes. In addition, SAR 4.0 W/kg amplified the number of apoptotic cells in the fly brain. These findings demonstrate that the exposure limit on electromagnetic radiation proposed by ANSI triggered ERK-survival signaling but the strong electromagnetic radiation activated JNK-apoptotic signaling in Drosophila.

(E) Lee W, Yang KL. Using medaka embryos as a model system to study biological effects of the electromagnetic fields on development and behavior. Ecotoxicol Environ Saf. 2014 Jul 29;108C:187-194. doi: 10.1016/j.ecoenv.2014.06.035. [Epub ahead of print]. (AS, CE, BE, DE, ME)

The electromagnetic fields (EMFs) of anthropogenic origin are ubiquitous in our environments. The health hazard of extremely low frequency and radiofrequency EMFs has been investigated for decades, but evidence remains inconclusive, and animal studies are urgently needed to resolve the controversies regarding developmental toxicity of EMFs. Furthermore, as undersea cables and technological devices are increasingly used, the lack of information regarding the health risk of EMFs to aquatic organisms needs to be addressed. Medaka embryos (Oryzias latipes) have been a useful tool to study developmental toxicity in vivo due to their optical transparency. Here we explored the feasibility of using medaka embryos as a model system to study biological effects of EMFs on development. We also used a white preference test to investigate behavioral consequences of the EMF developmental toxicity. Newly fertilized embryos were randomly assigned to four groups that were exposed to an EMF with 3.2 kHz at

the intensity of 0.12, 15, 25, or 60µT. The group exposed to the background 0.12µT served as the control. The embryos were exposed continually until hatch. They were observed daily, and the images were recorded for analysis of several developmental endpoints. Four days after hatching, the hatchlings were tested with the white preference test for their anxiety-like behavior. The results showed that embryos exposed to all three levels of the EMF developed significantly faster. The endpoints affected included the number of somites, eye width and length, eye pigmentation density, midbrain width, head growth, and the day to hatch. In addition, the group exposed to the EMF at 60µT exhibited significantly higher levels of anxiety-like behavior than the other groups did. In conclusion, the EMF tested in this study accelerated embryonic development and heightened anxiety-like behavior. Our results also demonstrate that the medaka embryo is a sensitive and cost-efficient in vivo model system to study developmental toxicity of EMFs.

(E) Leung S, Croft RJ, McKenzie RJ, Iskra S, Silber B, Cooper NR, O'Neill B, Cropley V, Diaz-Trujillo A, Hamblin D, Simpson D. Effects of 2G and 3G mobile phones on performance and electrophysiology in adolescents, young adults and older adults. Clin Neurophysiol. 122(11):2203-2216, 2011. (HU, AD, BE, EE)

OBJECTIVE: This study examined sensory and cognitive processing in adolescents, young adults and older adults, when exposed to 2nd (2G) and 3rd (3G) generation mobile phone signals. **METHODS:** Tests employed were the auditory 3-stimulus oddball and the N-back. Forty-one 13-15 year olds, forty-two 19-40 year olds and twenty 55-70 year olds were tested using a double-blind cross-over design, where each participant received Sham, 2G and 3G exposures, separated by at least 4 days. **RESULTS:** 3-Stimulus oddball task: Behavioural: accuracy and reaction time of responses to targets were not affected by exposure. Electrophysiological: augmented N1 was found in the 2G condition (independent of age group). N-back task: Behavioural: the combined groups performed less accurately during the 3G exposure (compared to Sham), with post hoc tests finding this effect separately in the adolescents only. Electrophysiological: delayed ERD/ERS responses of the alpha power were found in both 3G and 2G conditions (compared to Sham; independent of age group). **CONCLUSION:** Employing tasks tailored to each individual's ability level, this study provides support for an effect of acute 2G and 3G exposure on human cognitive function. **SIGNIFICANCE:** The subtlety of mobile phone effect on cognition in our study suggests that it is important to account for individual differences in future mobile phone research.

(E) Li H, Peng R, Wang C, Qiao S, Yong-Zou, Gao Y, Xu X, Wang S, Dong J, Zuo H, Li-Zhao, Zhou H, Wang L, Hu X. Alterations of cognitive function and 5-HT system in rats after long term microwave exposure. Physiol Behav. 40:236-246, 2015. (AS, CE, BE, CC, CH, EE, ME)

The increased use of microwaves raises concerns about its impact on health including cognitive function in which neurotransmitter system plays an important role. In this study, we focused on the serotonergic system and evaluated the long term effects of chronic microwave radiation on

cognition and correlated items. Wistar rats were exposed or sham exposed to 2.856GHz microwaves with the average power density of 5, 10, 20 or 30mW/cm^2 respectively for 6min three times a week up to 6weeks. At different time points after the last exposure, spatial learning and memory function, morphology structure of the hippocampus, electroencephalogram (EEG) and neurotransmitter content (amino acid and monoamine) of rats were tested. Above results raised our interest in serotonin system. Tryptophan hydroxylase 1 (TPH1) and monoamine oxidase (MAO), two important rate-limiting enzymes in serotonin synthesis and metabolic process respectively, were detected. Expressions of serotonin receptors including 5-HT$_{1A, 2A, 2C}$ receptors were measured. We demonstrated that chronic exposure to microwave (2.856GHz, with the average power density of 5, 10, 20 and 30mW/cm^2) could induce dose-dependent deficit of spatial learning and memory in rats accompanied with inhibition of brain electrical activity, the degeneration of hippocampus neurons, and the disturbance of neurotransmitters, among which the increase of 5-HT occurred as the main long-term change that the decrease of its metabolism partly contributed to. Besides, the variations of 5-HT$_{1A}$R and 5-HT$_{2C}$R expressions were also indicated. The results suggested that in the long-term way, chronic microwave exposure could induce cognitive deficit and 5-HT system may be involved in it.

(E) Li Y, Shi C, Lu G, Xu Q, Liu S. Effects of electromagnetic radiation on spatial memory and synapses in rat hippocampal CA1. Neural Regen Res. 7(16):1248-1255, 2012. (AS, CE, BE, ME)

In this study, we investigated the effects of mobile phone radiation on spatial learning, reference memory, and morphology in related brain regions. After the near-field radiation (0.52-1.08 W/kg) was delivered to 8-week-old Wistar rats 2 hours per day for 1 month, behavioral changes were examined using the Morris water maze. Compared with the sham-irradiated rats, the irradiated rats exhibited impaired performance. Morphological changes were investigated by examining synaptic ultrastructural changes in the hippocampus. Using the physical dissector technique, the number of pyramidal neurons, the synaptic profiles, and the length of postsynaptic densities in the CA1 region were quantified stereologically. The morphological changes included mitochondrial degenerations, fewer synapses, and shorter postsynaptic densities in the radiated rats. These findings indicate that mobile phone radiation can significantly impair spatial learning and reference memory and induce morphological changes in the hippocampal CA1 region.

(NE) Lipping T, Rorarius M, Jäntti V, Annala K, Mennander A, Ferenets R, Toivonen T, Toivo T, Värri A, Korpinen L. Using the nonlinear control of anaesthesia-induced hypersensitivity of EEG at burst suppression level to test the effects of radiofrequency radiation on brain function. Nonlinear Biomed Phys. 3(1):5, 2009. (AS, IA, EE)

BACKGROUND: In this study, investigating the effects of mobile phone radiation on test animals, eleven pigs were anaesthetised to the level where burst-suppression pattern appears in the electroencephalogram (EEG). At this level of anaesthesia both human subjects and animals show high sensitivity to external stimuli which produce EEG bursts during suppression. The burst-suppression phenomenon represents a nonlinear control system, where low-

amplitude EEG abruptly switches to very high amplitude bursts. This switching can be triggered by very minor stimuli and the phenomenon has been described as hypersensitivity. To test if also radio frequency (RF) stimulation can trigger this nonlinear control, the animals were exposed to pulse modulated signal of a GSM mobile phone at 890 MHz. In the first phase of the experiment electromagnetic field (EMF) stimulation was randomly switched on and off and the relation between EEG bursts and EMF stimulation onsets and endpoints were studied. In the second phase a continuous RF stimulation at 31 W/kg was applied for 10 minutes. The ECG, the EEG, and the subcutaneous temperature were recorded. **RESULTS:** No correlation between the exposure and the EEG burst occurrences was observed in phase I measurements. No significant changes were observed in the EEG activity of the pigs during phase II measurements although several EEG signal analysis methods were applied. The temperature measured subcutaneously from the pigs' head increased by 1.6 degrees C and the heart rate by 14.2 bpm on the average during the 10 min exposure periods. **CONCLUSION:** The hypothesis that RF radiation would produce sensory stimulation of somatosensory, auditory or visual system or directly affect the brain so as to produce EEG bursts during suppression was not confirmed.

(E) Liu ML, Wen JQ, Fan YB. Potential protection of green tea polyphenols against 1800 MHz electromagnetic radiation-induced injury on rat cortical neurons. Neurotox Res. 20(3):270-276, 2011. (CS, IA, CC, OX)

Radiofrequency electromagnetic fields (EMF) are harmful to public health, but the certain anti-irradiation mechanism is not clear yet. The present study was performed to investigate the possible protective effects of green tea polyphenols against electromagnetic radiation-induced injury in the cultured rat cortical neurons. In this study, green tea polyphenols were used in the cultured cortical neurons exposed to 1800 MHz EMFs by the mobile phone. We found that the mobile phone irradiation for 24 h induced marked neuronal cell death in the MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl-tetrazolium bromide) and TUNEL (TdT mediated biotin-dUTP nicked-end labeling) assay, and protective effects of green tea polyphenols on the injured cortical neurons were demonstrated by testing the content of Bcl-2 Assaciated X protein (Bax) in the immunoprecipitation assay and Western blot assay. In our study results, the mobile phone irradiation-induced increases in the content of active Bax were inhibited significantly by green tea polyphenols, while the contents of total Bax had no marked changes after the treatment of green tea polyphenols. Our results suggested a neuroprotective effect of green tea polyphenols against the mobile phone irradiation-induced injury on the cultured rat cortical neurons.

(E) Liu YX, Tai JL, Li GQ, Zhang ZW, Xue JH, Liu HS, Zhu H, Cheng JD, Liu YL, Li AM, Zhang Y. Exposure to 1950-MHz TD-SCDMA Electromagnetic Fields Affects the Apoptosis of Astrocytes via Caspase-3-Dependent Pathway. PLoS One. 7(8):e42332, 2012. (CS, CC)

The usage of mobile phone increases globally. However, there is still a paucity of data about the impact of electromagnetic fields (EMF) on human health. This study investigated whether EMF radiation would alter the biology of glial cells and act as a tumor-promoting agent. We exposed rat astrocytes and C6 glioma cells to 1950-MHz TD-SCDMA for 12, 24 and 48 h respectively, and

found that EMF exposure had differential effects on rat astroctyes and C6 glioma cells. A 48 h of exposure damaged the mitochondria and induced significant apoptosis of astrocytes. Moreover, caspase-3, a hallmark of apoptosis, was highlighted in astrocytes after 48 h of EMF exposure, accompanied by a significantly increased expression of bax and reduced level of bcl-2. The tumorigenicity assays demonstrated that astrocytes did not form tumors in both control and exposure groups. In contrast, the unexposed and exposed C6 glioma cells show no significant differences in both biological feature and tumor formation ability. Therefore, our results implied that exposure to the EMF of 1950-MHz TD-SCDMA may not promote the tumor formation, but continuous exposure damaged the mitochondria of astrocytes and induce apoptosis through a caspase-3-dependent pathway with the involvement of bax and bcl-2.

(E) López-Martín E, Bregains J, Relova-Quinteiro JL, Cadarso-Suárez C, Jorge-Barreiro FJ, Ares-Pena FJ. The action of pulse-modulated GSM radiation increases regional changes in brain activity and c-Fos expression in cortical and subcortical areas in a rat model of picrotoxin-induced seizure proneness. J Neurosci Res. 87(6):1484-1499, 2009. (AS, CC, WS)

The action of the pulse-modulated GSM radiofrequency of mobile phones has been suggested as a physical phenomenon that might have biological effects on the mammalian central nervous system. In the present study, GSM-exposed picrotoxin-pretreated rats showed differences in clinical and EEG signs, and in c-Fos expression in the brain, with respect to picrotoxin-treated rats exposed to an equivalent dose of unmodulated radiation. Neither radiation treatment caused tissue heating, so thermal effects can be ruled out. The most marked effects of GSM radiation on c-Fos expression in picrotoxin-treated rats were observed in limbic structures, olfactory cortex areas and subcortical areas, the dentate gyrus, and the central lateral nucleus of the thalamic intralaminar nucleus group. Nonpicrotoxin-treated animals exposed to unmodulated radiation showed the highest levels of neuronal c-Fos expression in cortical areas. These results suggest a specific effect of the pulse modulation of GSM radiation on brain activity of a picrotoxin-induced seizure-proneness rat model and indicate that this mobile-phone-type radiation might induce regional changes in previous preexcitability conditions of neuronal activation.

(E) Loughran SP, McKenzie RJ, Jackson ML, Howard ME, Croft RJ. Individual differences in the effects of mobile phone exposure on human sleep: rethinking the problem. Bioelectromagnetics. 33(1):86-93, 2012. (HU, EE, SL)

Mobile phone exposure-related effects on the human electroencephalogram (EEG) have been shown during both waking and sleep states, albeit with slight differences in the frequency affected. This discrepancy, combined with studies that failed to find effects, has led many to conclude that no consistent effects exist. We hypothesised that these differences might partly be due to individual variability in response, and that mobile phone emissions may in fact have large but differential effects on human brain activity. Twenty volunteers from our previous study underwent an adaptation night followed by two experimental nights in which they were randomly exposed to two conditions (Active and Sham), followed by a full-night sleep episode. The EEG spectral power was increased in the sleep spindle frequency range in the first 30 min

of non-rapid eye movement (non-REM) sleep following Active exposure. This increase was more prominent in the participants that showed an increase in the original study. These results confirm previous findings of mobile phone-like emissions affecting the EEG during non-REM sleep. Importantly, this low-level effect was also shown to be sensitive to individual variability. Furthermore, this indicates that previous negative results are not strong evidence for a lack of an effect and, given the far-reaching implications of mobile phone research, we may need to rethink the interpretation of results and the manner in which research is conducted in this field.

(NE) Loughran SP, Benz DC, Schmid MR, Murbach M, Kuster N, Achermann P. No increased sensitivity in brain activity of adolescents exposed to mobile phone-like emissions. Clin Neurophysiol. 124(7):1303-1308, 2013. (HU, BE, EE, AD)

OBJECTIVE: To examine the potential sensitivity of adolescents to radiofrequency electromagnetic field (RF EMF) exposures, such as those emitted by mobile phones. **METHODS:** In a double-blind, randomized, crossover design, 22 adolescents aged 11-13years (12 males) underwent three experimental sessions in which they were exposed to mobile phone-like RF EMF signals at two different intensities, and a sham session. During exposure cognitive tasks were performed and waking EEG was recorded at three time-points subsequent to exposure (0, 30 and 60min). **RESULTS:** No clear significant effects of RF EMF exposure were found on the waking EEG or cognitive performance. **CONCLUSIONS:** Overall, the current study was unable to demonstrate exposure-related effects previously observed on the waking EEG in adults, and also provides further support for a lack of an influence of mobile phone-like exposure on cognitive performance. **SIGNIFICANCE:** Adolescents do not appear to be more sensitive than adults to mobile phone RF EMF emissions.

(E) Lowden A, Akerstedt T, Ingre M, Wiholm C, Hillert L, Kuster N, Nilsson JP, Arnetz B. Sleep after mobile phone exposure in subjects with mobile phone-related symptoms. Bioelectromagnetics. 32(1):4-14, 2011. (HU, EE, SL)

Several studies show increases in activity for certain frequency bands (10-14 Hz) and visually scored parameters during sleep after exposure to radiofrequency electromagnetic fields. A shortened REM latency has also been reported. We investigated the effects of a double-blind radiofrequency exposure (884 MHz, GSM signaling standard including non-DTX and DTX mode, time-averaged 10 g psSAR of 1.4 W/kg) on self-evaluated sleepiness and objective EEG measures during sleep. Forty-eight subjects (mean age 28 years) underwent 3 h of controlled exposure (7:30-10:30 PM; active or sham) prior to sleep, followed by a full-night polysomnographic recording in a sleep laboratory. The results demonstrated that following exposure, time in Stages 3 and 4 sleep (SWS, slow-wave sleep) decreased by 9.5 min (12%) out of a total of 78.6 min, and time in Stage 2 sleep increased by 8.3 min (4%) out of a total of 196.3 min compared to sham. The latency to Stage 3 sleep was also prolonged by 4.8 min after exposure. Power density analysis indicated an enhanced activation in the frequency ranges 0.5-1.5 and 5.75-10.5 Hz during the first 30 min of Stage 2 sleep, with 7.5-11.75 Hz being elevated within the first hour of Stage 2 sleep, and bands 4.75-8.25 Hz elevated during the second hour of Stage 2 sleep. No pronounced power changes were observed in SWS or for the third hour of

scored Stage 2 sleep. No differences were found between controls and subjects with prior complaints of mobile phone-related symptoms. The results confirm previous findings that RF exposure increased the EEG alpha range in the sleep EEG, and indicated moderate impairment of SWS. Furthermore, reported differences in sensitivity to mobile phone use were not reflected in sleep parameters.

(E) Lu Y, Xu S, He M, Chen C, Zhang L, Liu C, Chu F, Yu Z, Zhou Z, Zhong M. Glucose administration attenuates spatial memory deficits induced by chronic low-power-density microwave exposure. Physiol Behav. 106(5):631-637, 2012. (AS, CE, BE)

Extensive evidence indicates that glucose administration attenuates memory deficits in rodents and humans, and cognitive impairment has been associated with reduced glucose metabolism and uptake in certain brain regions including the hippocampus. In the present study, we investigated whether glucose treatment attenuated memory deficits caused by chronic low-power-density microwave (MW) exposure, and the effect of MW exposure on hippocampal glucose uptake. We exposed Wistar rats to 2.45 GHz pulsed MW irradiation at a power density of 1 mW/cm(2) for 3 h/day, for up to 30 days. MW exposure induced spatial learning and memory impairments in rats. Hippocampal glucose uptake was also reduced by MW exposure in the absence or presence of insulin, but the levels of blood glucose and insulin were not affected. However, these spatial memory deficits were reversed by systemic glucose treatment. Our results indicate that glucose administration attenuates the spatial memory deficits induced by chronic low-power-density MW exposure, and reduced hippocampal glucose uptake may be associated with cognitive impairment caused by MW exposure.

(E) Lu Y, He M, Zhang Y, Xu S, Zhang L, He Y, Chen C, Liu C, Pi H, Yu Z, Zhou Z. Differential Pro-Inflammatory Responses of Astrocytes and Microglia Involve STAT3 Activation in Response to 1800 MHz Radiofrequency Fields. PLoS One. 2014 Oct 2;9(9):e108318. doi: 10.1371/journal.pone.0108318. (CS, CH)

Microglia and astrocytes play important role in maintaining the homeostasis of central nervous system (CNS). Several CNS impacts have been postulated to be associated with radiofrequency (RF) electromagnetic fields exposure. Given the important role of inflammation in neural physiopathologic processes, we investigated the pro-inflammatory responses of microglia and astrocytes and the involved mechanism in response to RF fields. Microglial N9 and astroglial C8-D1A cells were exposed to 1800 MHz RF for different time with or without pretreatment with STAT3 inhibitor. Microglia and astrocytes were activated by RF exposure indicated by up-regulated CD11b and glial fibrillary acidic protein (GFAP). However, RF exposure induced differential pro-inflammatory responses in astrocytes and microglia, characterized by different expression and release profiles of IL-1β, TNF-α, IL-6, PGE2, nitric oxide (NO), inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX2). Moreover, the RF exposure activated STAT3 in microglia but not in astrocytes. Furthermore, the STAT3 inhibitor Stattic ameliorated the RF-induced release of pro-inflammatory cytokines in microglia but not in astrocytes. Our results demonstrated that RF exposure differentially induced pro-inflammatory responses in

microglia and astrocytes, which involved differential activation of STAT3 in microglia and astrocytes. Our data provide novel insights into the potential mechanisms of the reported CNS impacts associated with mobile phone use and present STAT3 as a promising target to protect humans against increasing RF exposure.

(E) Luria R, Eliyahu I, Hareuveny R, Margaliot M, Meiran N. Cognitive effects of radiation emitted by cellular phones: the influence of exposure side and time. Bioelectromagnetics. 30(3):198-204, 2009. (See also Hareuveny et al., 2011) (HU, BE)

This study examined the time dependence effects of exposure to radiofrequency radiation (RFR) emitted by standard GSM cellular phones on the cognitive functions of humans. A total of 48 healthy right-handed male subjects performed a spatial working memory task (that required either a left-hand or a right-hand response) while being exposed to one of two GSM phones placed at both sides of the head. The subjects were randomly divided into three groups. Each group was exposed to one of three exposure conditions: left-side of the head, right-side, or sham-exposure. The experiment consisted of 12 blocks of trials. Response times (RTs) and accuracy of the responses were recorded. It was found that the average RT of the right-hand responses under left-side exposure condition was significantly longer than those of the right-side and sham-exposure groups averaged together during the first two time blocks. These results confirmed the existence of an effect of exposure on RT, as well as the fact that exposure duration (together with the responding hand and the side of exposure) may play an important role in producing detectable RFR effects on performance. Differences in these parameters might be the reason for the failure of certain studies to detect or replicate RFR effects.

(E) Lustenberger C, Murbach M, Durr R, Schmid MR, Kuster N, Achermann P, Huber R. Stimulation of the brain with radiofrequency electromagnetic field pulses affects sleep-dependent performance improvement. Brain Stimul 6(5):805-811, 2013. (HU, BE, EE, SL)

Background: Sleep-dependent performance improvements seem to be closely related to sleep spindles (12–15 Hz) and sleep slow-wave activity (SWA, 0.75–4.5 Hz). Pulse-modulated radiofrequency electromagnetic fields (RF EMF, carrier frequency 900 MHz) are capable to modulate these electroencephalographic (EEG) characteristics of sleep. Objective: The aim of our study was to explore possible mechanisms how RF EMF affects cortical activity during sleep and to test whether such effects on cortical activity during sleep interact with sleep-dependent performance changes. Methods: Sixteen male subjects underwent 2 experimental nights, one of them with all-night 0.25–0.8 Hz pulsed RF EMF exposure. All-night EEG was recorded. To investigate RF EMF induced changes in overnight performance improvement, subjects were trained for both nights on a motor task in the evening and the morning. Results: We obtained good sleep quality in all subjects under both conditions (mean sleep efficiency > 90%). After pulsed RF EMF we found increased SWA during exposure to pulse-modulated RF EMF compared to sham exposure ($P < 0.05$) toward the end of the sleep period. Spindle activity was not

affected. Moreover, subjects showed an increased RF EMF burst-related response in the SWA range, indicated by an increase in event-related EEG spectral power and phase changes in the SWA range. Notably, during exposure, sleep-dependent performance improvement in the motor sequence task was reduced compared to the sham condition (−20.1%, *P* = 0.03). Conclusion: The changes in the time course of SWA during the exposure night may reflect an interaction of RF EMF with the renormalization of cortical excitability during sleep, with a negative impact on sleep-dependent performance improvement.

(E) Lustenberger, C., Murbach, M., Tüshaus, L., Wehrle, F., Kuster, N., Achermann, P. and Huber, R., Inter-individual and intra-individual variation of the effects of pulsed RF EMF exposure on the human sleep EEG. Bioelectromagnetics. 36(3) 169, 2015. (HU, EE)

Pulse-modulated radiofrequency electromagnetic fields (RF EMF) can alter brain activity during sleep; increases of electroencephalographic (EEG) power in the sleep spindle (13.75–15.25 Hz) and delta-theta (1.25–9 Hz) frequency range have been reported. These field effects show striking inter-individual differences. However, it is still unknown whether individual subjects react in a similar way when repeatedly exposed. Thus, our study aimed to investigate inter-individual variation and intra-individual stability of field effects. To do so, we exposed 20 young male subjects twice for 30 min prior to sleep to the same amplitude modulated 900 MHz (2 Hz pulse, 20 Hz Gaussian low-pass filter and a ratio of peak-to-average of 4) RF EMF (spatial peak absorption of 2 W/kg averaged over 10 g) 2 weeks apart. The topographical analysis of EEG power during all-night non-rapid eye movement sleep revealed: (1) exposure-related increases in delta-theta frequency range in several fronto-central electrodes; and (2) no differences in spindle frequency range. We did not observe reproducible within-subject RF EMF effects on sleep spindle and delta-theta activity in the sleep EEG and it remains unclear whether a biological trait of how the subjects' brains react to RF EMF exists.

(E) Lv B, Chen Z, Wu T, Shao Q, Yan D, Ma L, Lu K, Xie Y. The alteration of spontaneous low frequency oscillations caused by acute electromagnetic fields exposure. Clin Neurophysiol. 125:277-286, 2014. (HU, EE, PE)

OBJECTIVE: The motivation of this study is to evaluate the possible alteration of regional resting state brain activity induced by the acute radiofrequency **electromagnetic** field (RF-EMF) exposure (30min) of Long Term Evolution (LTE) signal. METHODS: We designed a controllable near-field LTE RF-EMF exposure environment. Eighteen subjects participated in a double-blind, crossover, randomized and counterbalanced experiment including two sessions (real and sham exposure). The radiation source was close to the right ear. Then the resting state fMRI signals of human brain were collected before and after the exposure in both sessions. We measured the amplitude of low frequency fluctuation (ALFF) and fractional ALFF (fALFF) to characterize the spontaneous brain activity. RESULTS: We found the decreased ALFF value around in left superior temporal gyrus, left middle temporal gyrus, right superior temporal gyrus, right medial frontal gyrus and right paracentral lobule after the real exposure. And the decreased fALFF

value was also detected in right medial frontal gyrus and right paracentral lobule. CONCLUSIONS: The study provided the evidences that 30min LTE RF-EMF exposure modulated the spontaneous low frequency fluctuations in some brain regions. SIGNIFICANCE: With resting state fMRI, we found the alteration of spontaneous low frequency fluctuations induced by the acute LTE RF-EMF exposure.

(E) Lv B, Su C, Yang L, Xie Y, Wu T. Whole brain EEG synchronization likelihood modulated by long term evolution electromagnetic fields exposure. Conf Proc IEEE Eng Med Biol Soc. 2014:986-989, 2014. (HU, EE)

In this paper, we aimed to investigate the possible interactions between human brain and radiofrequency electromagnetic fields (EMF) with electroencephalogram (EEG) technique. Unlike the previous studies which mainly focused on EMF effect on local brain activities, we attempted to evaluate whether the EMF emitted from Long Term Evolution (LTE) devices can modulate the functional connectivity of brain electrical activities. Ten subjects were recruited to participate in a crossover, double-blind exposure experiment which included two sessions (real and sham exposure). In each session, LTE EMF exposure (power on or off) lasted for 30 min and the EEG signals were collected with 32 channels throughout the experiment. Then we applied the synchronization likelihood method to quantify the neural synchronization over the whole brain in different frequency bands and in different EEG record periods. Our results illustrated that the short-term LTE EMF exposure would modulate the synchronization patterns of EEG activation across the whole brain.

(E) Maaroufi K, Had-Aissouni L, Melon C, Sakly M, Abdelmelek H, Poucet B, Save E. Spatial learning, monoamines and oxidative stress in rats exposed to 900MHz electromagnetic field in combination with iron overload. Behav Brain Res. 258:80-89, 2014. (AS, CE, BE, CH)

The increasing use of mobile phone technology over the last decade raises concerns about the impact of high frequency electromagnetic fields (EMF) on health. More recently, a link between EMF, iron overload in the brain and neurodegenerative disorders including Parkinson's and Alzheimer's diseases has been suggested. Co-exposure to EMF and brain iron overload may have a greater impact on brain tissues and cognitive processes than each treatment by itself. To examine this hypothesis, Long-Evans rats submitted to 900MHz exposure or combined 900MHz EMF and iron overload treatments were tested in various spatial learning tasks (navigation task in the Morris water maze, working memory task in the radial-arm maze, and object exploration task involving spatial and non spatial processing). Biogenic monoamines and metabolites (dopamine, serotonin) and oxidative stress were measured. Rats exposed to EMF were impaired in the object exploration task but not in the navigation and working memory tasks. They also showed alterations of monoamine content in several brain areas but mainly in the hippocampus. Rats that received combined treatment did not show greater behavioral and neurochemical deficits than EMF-exposed rats. None of the two treatments produced global

oxidative stress. These results show that there is an impact of EMF on the brain and cognitive processes but this impact is revealed only in a task exploiting spontaneous exploratory activity. In contrast, there are no synergistic effects between EMF and a high content of iron in the brain.

(E) Maganioti AE, Hountala CD, Papageorgiou CC, Kyprianou MA, Rabavilas AD, Capsalis CN. Principal component analysis of the P600 waveform: RF and gender effects. Neurosci Lett. 478(1):19-23, 2010. (HU, EE)

The aim of the present study was to examine the patterns of activation of the P600 waveform of the event-related potentials (ERP), applying principal component analysis (PCA) and repeated measures ANOVA, and whether these patterns are RF and gender dependent. The ERPs of thirty-nine healthy subjects (20 male and 19 female) were recorded during an auditory memory task in the presence and absence of RF, similar to that emitted by mobile phones. Both PCA and ANOVA produced congruent results, showing that activation of the P600 component occurs early and more intensely in the region of the posterior electrodes and in a less intense manner in the central electrodes. Conversely, the activation at the anterior electrodes arises later with a considerably reduced intensity. In the absence of RF female subjects exhibited significantly lower amplitudes at anterior electrodes and earlier latencies at central electrodes than male subjects. These differences disappear in the presence of RF. Consequently, the P600 component follows distinct patterns of activation in the anterior, central and posterior brain areas and gender differences are observed simultaneously at several electrodes within these areas. Finally, the gender-related functional architecture with regard the P600 component appears to be RF sensitive. In conclusion, the application of the PCA procedure provides an adequate model of the spatially distributed event-related dynamics that correspond to the P600 waveform.

(NE) Malek F, Rani KA, Rahim HA, Omar MH. Effect of Short-Term Mobile Phone Base Station Exposure on Cognitive Performance, Body Temperature, Heart Rate and Blood Pressure of Malaysians. Sci Rep. 5:13206, 2015. (HU, BE)

Individuals who report their sensitivity to electromagnetic fields often undergo cognitive impairments that they believe are due to the exposure of mobile phone technology. The aim of this study is to clarify whether short-term exposure at 1 V/m to the typical Global System for Mobile Communication and Universal Mobile Telecommunications System (UMTS) affects cognitive performance and physiological parameters (body temperature, blood pressure and heart rate). This study applies counterbalanced randomizing single blind tests to determine if sensitive individuals experience more negative health effects when they are exposed to base station signals compared with sham (control) individuals. The sample size is 200 subjects with 50.0% Idiopathic Environmental Intolerance attributed to electromagnetic fields (IEI-EMF) also known as sensitive and 50.0% (non-IEI-EMF). The computer-administered Cambridge Neuropsychological Test Automated Battery (CANTAB eclipse(TM)) is used to examine cognitive performance. Four tests are chosen to evaluate Cognitive performance in CANTAB: Reaction Time (RTI), Rapid Visual Processing (RVP), Paired Associates Learning (PAL) and Spatial Span

(SSP). Paired sample t-test on the other hand, is used to examine the physiological parameters. Generally, in both groups, there is no statistical significant difference between the exposure and sham exposure towards cognitive performance and physiological effects (P's > 0.05).

(E) Malkemper EP, Eder SH, Begall S, Phillips JB, Winklhofer M, Hart V, Burda H. Magnetoreception in the wood mouse (Apodemus sylvaticus): influence of weak frequency-modulated radio frequency fields. Sci Rep. 2015 Apr 29;4:9917. doi: 10.1038/srep09917. (AS, LI, BE)

The mammalian magnetic sense is predominantly studied in species with reduced vision such as mole-rats and bats. Far less is known about surface-dwelling (epigeic) rodents with well-developed eyes. Here, we tested the wood mouse Apodemus sylvaticus for magnetoreception using a simple behavioural assay in which mice are allowed to build nests overnight in a visually symmetrical, circular arena. The tests were performed in the ambient magnetic field or in a field rotated by 90°. When plotted with respect to magnetic north, the nests were bimodally clustered in the northern and southern sectors, clearly indicating that the animals used magnetic cues. Additionally, mice were tested in the ambient magnetic field with a superimposed radio frequency magnetic field of the order of 100 nT. Wood mice exposed to a 0.9 to 5 MHz frequency sweep changed their preference from north-south to east-west. In contrast to birds, however, a constant frequency field tuned to the Larmor frequency (1.33 MHz) had no effect on mouse orientation. In sum, we demonstrated magnetoreception in wood mice and provide first evidence for a radical-pair mechanism in a mammal.

(E) Mandalà M, Colletti V, Sacchetto L, Manganotti P, Ramat S, Marcocci A, Colletti L. Effect of Bluetooth headset and mobile phone electromagnetic fields on the human auditory nerve. Laryngoscope. 124:255-259, 2014. (HU, EE)

OBJECTIVES/HYPOTHESIS: The possibility that long-term mobile phone use increases the incidence of astrocytoma, glioma and acoustic neuroma has been investigated in several studies. Recently, our group showed that direct exposure (in a surgical setting) to cell phone electromagnetic fields (EMFs) induces deterioration of auditory evoked cochlear nerve compound action potential (CNAP) in humans. To verify whether the use of Bluetooth devices reduces these effects, we conducted the present study with the same experimental protocol. STUDY DESIGN: Randomized trial. METHODS: Twelve patients underwent retrosigmoid vestibular neurectomy to treat definite unilateral Ménière's disease while being monitored with acoustically evoked CNAPs to assess direct mobile phone exposure or alternatively the EMF effects of Bluetooth headsets. RESULTS: We found no short-term effects of Bluetooth EMFs on the auditory nervous structures, whereas direct mobile phone EMF exposure confirmed a significant decrease in CNAPs amplitude and an increase in latency in all subjects. CONCLUSIONS: The outcomes of the present study show that, contrary to the finding that the latency and amplitude of CNAPs are very sensitive to EMFs produced by the tested mobile phone, the EMFs produced by a common Bluetooth device do not induce any significant change in cochlear nerve activity. The conditions of exposure, therefore, differ from those of everyday

life, in which various biological tissues may reduce the EMF affecting the cochlear nerve. Nevertheless, these novel findings may have important safety implications.

(E) Maskey D, Kim M, Aryal B, Pradhan J, Choi IY, Park KS, Son T, Hong SY, Kim SB, Kim HG, Kim MJ. Effect of 835 MHz radiofrequency radiation exposure on calcium binding proteins in the hippocampus of the mouse brain. Brain Res. 1313:232-241, 2010a. (AS, CE, ME, CH)

Worldwide expansion of mobile phones and electromagnetic field (EMF) exposure has raised question of their possible biological effects on the brain and nervous system. Radiofrequency (RF) radiation might alter intracellular signaling pathways through changes in calcium (Ca(2+)) permeability across cell membranes. Changes in the expression of calcium binding proteins (CaBP) like calbindin D28-k (CB) and calretinin (CR) could indicate impaired Ca(2+)homeostasis due to EMF exposure. CB and CR expression were measured with immunohistochemistry in the hippocampus of mice after EMF exposure at 835 MHz for different exposure times and absorption rates, 1 h/day for 5 days at a specific absorption rate (SAR)=1.6 W/kg, 1 h/day for 5 days at SAR=4.0 W/kg, 5 h/day for 1 day at SAR=1.6 W/kg, 5 h/day for 1 day at SAR=4.0 W/kg, daily exposure for 1 month at SAR=1.6 W/kg. Body weights did not change significantly. CB immunoreactivity (IR) displayed moderate staining of cells in the cornu ammonis (CA) areas and prominently stained granule cells. CR IR revealed prominently stained pyramidal cells with dendrites running perpendicularly in the CA area. Exposure for 1 month produced almost complete loss of pyramidal cells in the CA1 area. CaBP differences could cause changes in cellular Ca(2+)levels, which could have deleterious effect on normal hippocampal functions concerned with neuronal connectivity and integration.

(E) Maskey D, Pradhan J, Aryal B, Lee CM, Choi IY, Park KS, Kim SB, Kim HG, Kim MJ. Chronic 835-MHz radiofrequency exposure to mice hippocampus alters the distribution of calbindin and GFAP immunoreactivity. Brain Res. 1346:237-246, 2010b. (AS, CE, ME, CH)

Exponential interindividual handling in wireless communication system has raised possible doubts in the biological aspects of radiofrequency (RF) exposure on human brain owing to its close proximity to the mobile phone. In the nervous system, calcium (Ca(2+)) plays a critical role in releasing neurotransmitters, generating action potential and membrane integrity. Alterations in intracellular Ca(2+) concentration trigger aberrant synaptic action or cause neuronal apoptosis, which may exert an influence on the cellular pathology for learning and memory in the hippocampus. Calcium binding proteins like calbindin D28-K (CB) is responsible for the maintaining and controlling Ca(2+) homeostasis. Therefore, in the present study, we investigated the effect of RF exposure on rat hippocampus at 835 MHz with low energy (specific absorption rate: SAR=1.6 W/kg) for 3 months by using both CB and glial fibrillary acidic protein (GFAP) specific antibodies by immunohistochemical method. Decrease in CB immunoreactivity (IR) was noted in exposed (E1.6) group with loss of interneurons and pyramidal cells in CA1 area and loss of granule cells. Also, an overall increase in GFAP IR was observed in the hippocampus of E1.6. By TUNEL assay, apoptotic cells were detected in the CA1, CA3 areas and dentate gyrus of hippocampus, which reflects that chronic RF exposure may affect the cell viability. In addition, the increase of GFAP IR due to RF exposure could be well suited with the feature of

reactive astrocytosis, which is an abnormal increase in the number of astrocytes due to the loss of nearby neurons. Chronic RF exposure to the rat brain suggested that the decrease of CB IR accompanying apoptosis and increase of GFAP IR might be morphological parameters in the hippocampus damages.

(E) Maskey D, Kim HJ, Kim HG, Kim MJ. Calcium-binding proteins and GFAP immunoreactivity alterations in murine hippocampus after 1 month of exposure to 835 MHz radiofrequency at SAR values of 1.6 and 4.0 W/kg. Neurosci Lett. 506(2):292-296, 2012. (AS, CE, ME, CH)

Widespread use of wireless mobile communication has raised concerns of adverse effect to the brain owing to the proximity during use due to the electromagnetic field emitted by mobile phones. Changes in calcium ion concentrations via binding proteins can disturb calcium homeostasis; however, the correlation between calcium-binding protein (CaBP) immunoreactivity (IR) and glial cells has not been determined with different SAR values. Different SAR values [1.6 (E1.6 group) and 4.0 (E4 group) W/kg] were applied to determine the distribution of calbindin D28-k (CB), calretinin (CR), and glial fibrillary acidic protein (GFAP) IR in murine hippocampus. Compared with sham control group, decreased CB and CR IRs, loss of CB and CR immunoreactive cells and increased GFAP IR exhibiting hypertrophic cytoplasmic processes were noted in both experimental groups. E4 group showed a prominent decrement in CB and CR IR than the E1.6 group due to down-regulation of CaBP proteins and neuronal loss. GFAP IR was more prominent in the E4 group than the E1.6 group. Decrement in the CaBPs can affect the calcium-buffering capacity leading to cell death, while increased GFAP IR and changes in astrocyte morphology, may mediate brain injury due to radiofrequency exposure.

(E) Maskey D, Kim MJ. Immunohistochemical Localization of Brain-derived Neurotrophic Factor and Glial Cell Line-derived Neurotrophic Factor in the Superior Olivary Complex of Mice after Radiofrequency Exposure. Neuroscience Letters. 564:78-82, 2014. (AS, CE, CH)

Raising health concerns about the biological effects from radiofrequency exposure, even with conflicting results, has prompted calls for formulation of a guideline of the biological safety level. Given the close proximity between a mobile phone and the ear, it has been suggested that the central auditory system may be detrimentally influenced by radiofrequency exposure. In the auditory system, neurotrophins are important in the regulation of neuron survival, especially mammalian cochlear neurons. Neurotrophic factors like brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF) present in the auditory system are responsible for the maintenance of auditory neurons. BDNF and GDNF may protect against acoustic trauma and prevent from hearing defect. The present study applied radiofrequency at a specific absorption rate (SAR) of 1.6 W/kg (E1.6) or 0 W/kg group to determine the distribution of BDNF and GDNF in the nuclei of superior olivary complex (SOC). In the E1.6 group, significant decrements of BDNF immunoreactivity (IR) were noted in the lateral superior olive, medial superior olive, superior paraolivary nucleus and medial nucleus of the trapezoid body. GDNF IR was also significantly decreased ($p < 0.001$) in all SOC nuclei of the E1.6 group. The decrease in the IR of these neurotrophic factors in the SOC of the E1.6 group suggests a detrimental effect of RF exposure in the auditory nuclei.

(NE) Masuda H, Ushiyama A, Takahashi M, Wang J, Fujiwara O, Hikage T, Nojima T, Fujita K, Kudo M, Ohkubo C. Effects of 915 MHz electromagnetic-field radiation in TEM cell on the blood-brain barrier and neurons in the rat brain. Radiat Res. 172(1):66-73, 2009. (AS, ME)

The aim of this study was to determine whether albumin leakage and dark neurons were present in rat brains 14 and 50 days after a single 2-h exposure to a 915 MHz electromagnetic field, as reported by Salford et al. (Environ. Health Perspect. 111, 881-883, 203). Sixty-four male F344 rats (12 weeks old) were exposed to a 915 MHz electromagnetic field at whole-body average specific absorption rates of 0, 0.02, 0.2 and 2.0 W/kg in TEM cells for 2 h, following the protocol reported by Salford et al. The brains were examined histologically and immunohistochemically. No albumin immunoreactivity was observed in the exposed groups. In addition, dark neurons, assessed using hematoxylin and eosin staining, were rarely present, with no statistically significant difference between exposed and sham-exposed animals. This study thus failed to confirm the results of Salford et al.

(E) Masuda H, Hirata A, Kawai H, Wake K, Watanabe S, Arima T, Poulletier de Gannes F, Lagroye I, Veyret B. Local exposure of the rat cortex to radiofrequency electromagnetic fields increases local cerebral blood flow along with temperature. J Appl Physiol. 110(1):142-148, 2011. (AS, PE)

Few studies have shown that local exposure to radiofrequency electromagnetic fields (RF) induces intensity-dependent physiological changes, especially in the brain. The aim of the present study was to detect reproducible responses to local RF exposure in the parietal cortex of anesthetized rats and to determine their dependence on RF intensity. The target cortex tissue was locally exposed to 2-GHz RF using a figure-eight loop antenna within a range of averaged specific absorption rates (10.5, 40.3, 130, and 263 W/kg averaged over 4.04 mg) in the target area. Local cerebral blood flow (CBF) and temperatures in three regions (target area, rectum, and calf hypodermis) were measured using optical fiber blood flow meters and thermometers during RF exposure. All parameters except for the calf hypodermis temperature increased significantly in exposed animals compared with sham-exposed ones during 18-min exposures. Dependence of parameter values on exposure intensity was analyzed using linear regression models. The elevation of local CBF was correlated with temperature rise in both target and rectum at the end of RF exposure. However, the local CBF elevation seemed to be elevated by the rise in target temperature, but not by that of the rectal temperature, in the early part of RF exposure or at low-intensity RF exposure. These findings suggest that local RF exposure of the rat cortex drives a regulation of CBF accompanied by a local temperature rise, and our findings may be helpful for discussing physiological changes in the local cortex region, which is locally exposed to RF.

(NE) Masuda H, Hirota S, Ushiyama A, Hirata A, Arima T, Watanabe H, Wake K, Watanabe S, Taki M, Nagai A, Ohkubo C. No Changes in Cerebral Microcirculatory Parameters in Rat During Local Cortex Exposure to Microwaves. In Vivo. 29(2):207-215, 2015. (AS, PE)

The aim of this study was to determine whether cerebral microcirculatory parameters in rats were modified during local cortex exposure to a radiofrequency electromagnetic field (RF) under non-thermal conditions. The cortex tissue targeted was locally exposed to 1439 MHz RF using a figure-8 loop antenna at an averaged specific absorption rate of 2.0 W/kg in the target area for 50 min. Three microcirculatory parameters related to cerebral inflammation were measured by the cranial window method in real-time under RF exposure. No extravasation of intravenously injected fluorescent dye was observed during RF exposure. There was no significant difference either in pial venule blood flow velocity or diameter between exposed and sham-exposed rats. Histological evaluation for the brain immediately after RF exposure did not reveal any serum albumin leakage sites or degenerate neurons. These findings suggest that no dynamic changes occurred in cerebral microcirculation even during local cortex exposure under these conditions.

(E) Mathur R. Effect of chronic intermittent exposure to AM radiofrequency field on responses to various types of noxious stimuli in growing rats. Electromagn Biol Med. 27(3):266-276, 2008. (AS, CE, BE)

There are several reports of altered pain sensation after exposure (from a few minutes to hours in single or repeated doses for 2-3 weeks) to electromagnetic fields (EMF) in adults. The commonly utilized noxious stimulus is radiant heat. The nociceptive responses are known to be influenced by characteristics of stimulus, organism, and environment. We studied the pattern of nociceptive responses to various noxious stimuli in growing rats exposed to radiofrequency field (73.5 MHz amplitude modulated, 16 Hz power density 1.33 mw/cm(2), SAR = 0.4 w/kg) for 45 d (2 h/d). Threshold current for stimulation of nociceptive afferents to mediate motor response of tail (TF), vocalization during stimulus (VD), and vocalization after discharge (VA); the withdrawal latency of tail (TFL) and hind paw (HPL) to thermal noxious stimulus and tonic pain responses were recorded in every rat. The TFL was not affected, HPL was decreased ($p < 0.01$), and the thresholds of TF and VD were not affected, while, that of VA was significantly decreased. The tonic pain rating was decreased ($p < 0.01$). A decrease in the threshold of VA ($p < 0.01$) is indicative of an increase in the emotional component of the response to the phasic pain, whereas a decrease in the pain rating indicates analgesia in response to the tonic pain. The results of our study suggest that chronic (45 d), intermittent (2 h/d) amplitude modulated RF field exposure to the peripubertal rat increases the emotional component of phasic pain over a basal eaualgesic state, while late response to tonic pain is decreased. The data suggest that amplitude modulated RF field differentially affects the mechanisms involved in the processing of various noxious stimuli.

(NE) McNamee JP, Bellier PV, Konkle AT, Thomas R, Wasoontarajaroen S, Lemay E, Gajda GB. Analysis of gene expression in mouse brain regions after exposure to 1.9 GHz radiofrequency fields. Int J Radiat Biol. 2016 Mar 30:1-13. [Epub ahead of print] (AS, CE, CH)

PURPOSE: To assess 1.9 GHz radiofrequency (RF) field exposure on gene expression within a variety of discrete mouse brain regions using whole genome microarray analysis MATERIALS AND METHODS: Adult male C57BL/6 mice were exposed to 1.9 GHz pulse-modulated or

continuous-wave RF fields for 4 h/day for 5 consecutive days at whole body average (WBA) specific absorption rates of 0 (sham), ~0.2 W/kg and ~1.4 W/kg. Total RNA was isolated from the auditory cortex, amygdala, caudate, cerebellum, hippocampus, hypothalamus, and medial prefrontal cortex and differential gene expression was assessed using Illumina MouseWG-6 (v2) BeadChip arrays. Validation of potentially responding genes was conducted by RT-PCR. RESULTS: When analysis of gene expression was conducted within individual brain regions when controlling the false discovery rate (FDR), no differentially expressed genes were identified relative to the sham control. However, it must be noted that most fold changes among groups were observed to be less than 1.5-fold and this study had limited ability to detect such small changes. While some genes were differentially expressed without correction for multiple-comparisons testing, no consistent pattern of response was observed among different RF-exposure levels or among different RF-modulations. CONCLUSIONS: The current study provides the most comprehensive analysis of potential gene expression changes in the rodent brain in response to RF field exposure conducted to date. Within the exposure conditions and limitations of this study, no convincing evidence of consistent changes in gene expression was found in response to 1.9 GHz RF field exposure.

(E) Megha K, Deshmukh PS, Banerjee BD, Tripathi AK, Abegaonkar MP. Microwave radiation induced oxidative stress, cognitive impairment and inflammation in brain of Fischer rats. Indian J Exp Biol. 50(12):889-896, 2012. (AS, LI, CE, BE, OX, CH)

Public concerns over possible adverse effects of microwave radiation emitted by mobile phones on health are increasing. To evaluate the intensity of oxidative stress, cognitive impairment and inflammation in brain of Fischer rats exposed to microwave radiation, male Fischer-344 rats were exposed to 900 MHz microwave radiation (SAR = 5.953 x 10(-4) W/kg) and 1800 MHz microwave radiation (SAR = 5.835 x 10(-4) W/kg) for 30 days (2 h/day). Significant impairment in cognitive function and induction of oxidative stress in brain tissues of microwave exposed rats were observed in comparison with sham exposed groups. Further, significant increase in level of cytokines (IL-6 and TNF-alpha) was also observed following microwave exposure. Results of the present study indicated that increased oxidative stress due to microwave exposure may contribute to cognitive impairment and inflammation in brain.

(E) Megha K, Deshmukh PS, Ravi AK, Tripathi AK, Abegaonkar MP, Banerjee BD. Effect of Low-Intensity Microwave Radiation on Monoamine Neurotransmitters and Their Key Regulating Enzymes in Rat Brain. Cell Biochem Biophys. 73:93-100, 2015. (AS, LI, CE, CH)

The increasing use of wireless communication devices has raised major concerns towards deleterious effects of microwave radiation on human health. The aim of the study was to demonstrate the effect of low-intensity microwave radiation on levels of monoamine neurotransmitters and gene expression of their key regulating enzymes in brain of Fischer rats. Animals were exposed to 900 MHz and 1800 MHz microwave radiation for 30 days (2 h/day, 5 days/week) with respective specific absorption rates as 5.953×10^{-4} and 5.835×10^{-4} W/kg. The levels of monoamine neurotransmitters viz. dopamine (DA), norepinephrine (NE),

epinephrine (E) and serotonin (5-HT) were detected using LC-MS/MS in hippocampus of all experimental animals. In addition, mRNA expression of key regulating enzymes for these neurotransmitters viz. tyrosine hydroxylase (TH) (for DA, NE and E) and tryptophan hydroxylase (TPH1 and TPH2) (for serotonin) was also estimated. Results showed significant reduction in levels of DA, NE, E and 5-HT in hippocampus of microwave-exposed animals in comparison with sham-exposed (control) animals. In addition, significant downregulation in mRNA expression of TH, TPH1 and TPH2 was also observed in microwave-exposed animals ($p < 0.05$). In conclusion, the results indicate that low-intensity microwave radiation may cause learning and memory disturbances by altering levels of brain monoamine neurotransmitters at mRNA and protein levels.

(E) Meral I, Mert H, Mert N, Deger Y, Yoruk I, Yetkin A, Keskin S. Effects of 900-MHz electromagnetic field emitted from cellular phone on brain oxidative stress and some vitamin levels of guinea pigs. Brain Res. 1169:120-124, 2007. (AS, CE, OX)

This study was designed to demonstrate the effects of 900-MHz electromagnetic field (EMF) emitted from cellular phone on brain tissue and also blood malondialdehyde (MDA), glutathione (GSH), retinol (vitamin A), vitamin D(3) and tocopherol (vitamin E) levels, and catalase (CAT) enzyme activity of guinea pigs. Fourteen male guinea pigs, weighing 500-800 g were randomly divided into one of two experimental groups: control and treatment (EMF-exposed), each containing seven animals. Animals in treatment group were exposed to 890- to 915-MHz EMF (217-Hz pulse rate, 2-W maximum peak power, SAR 0.95 w/kg) of a cellular phone for 12 h/day (11-h 45-min stand-by and 15-min spiking mode) for 30 days. Control guinea pigs were housed in a separate room without exposing EMF of a cellular phone. Blood samples were collected through a cardiac puncture and brains were removed after decapitation for the biochemical analysis at the end of the 30 days of experimental period. It was found that the MDA level increased ($P<0.05$), GSH level and CAT enzyme activity decreased ($P<0.05$), and vitamins A, E and D(3) levels did not change ($P>0.05$) in the brain tissues of EMF-exposed guinea pigs. In addition, MDA, vitamins A, D(3) and E levels, and CAT enzyme activity increased ($P<0.05$), and GSH level decreased ($P<0.05$) in the blood of EMF-exposed guinea pigs. It was concluded that electromagnetic field emitted from cellular phone might produce oxidative stress in brain tissue of guinea pigs. However, more studies are needed to demonstrate whether these effects are harmful or/and affect the neural functions.

(NE) Mohler E, Frei P, Braun-Fahrländer C, Fröhlich J, Neubauer G, Röösli M; Qualifex Team. Effects of everyday radiofrequency electromagnetic-field exposure on sleep quality: a cross-sectional study. Radiat Res. 174(3):347-356, 2010. (HU, SL)

The aim of this cross-sectional study was to investigate the association between exposure to various sources of radiofrequency electromagnetic fields (RF EMFs) in the everyday environment and sleep quality, which is a common public health concern. We assessed self-reported sleep disturbances and daytime sleepiness in a random population sample of 1,375 inhabitants from the area of Basel, Switzerland. Exposure to environmental far-field RF EMFs was predicted for each individual using a prediction model that had been developed and

validated previously. Self-reported cordless and mobile phone use as well as objective mobile phone operator data for the previous 6 months were also considered in the analyses. In multivariable regression models, adjusted for relevant confounders, no associations between environmental far-field RF EMF exposure and sleep disturbances or excessive daytime sleepiness were observed. The 10% most exposed participants had an estimated risk for sleep disturbances of 1.11 (95% CI: 0.50 to 2.44) and for excessive daytime sleepiness of 0.58 (95% CI: 0.31 to 1.05). Neither mobile phone use nor cordless phone use was associated with decreased sleep quality. The results of this large cross-sectional study did not indicate an impairment of subjective sleep quality due to exposure from various sources of RF EMFs in everyday life.

(NE) Mohler E, Frei P, Fröhlich J, Braun-Fahrländer C, Röösli M; QUALIFEX-team. Exposure to radiofrequency electromagnetic fields and sleep quality: a prospective cohort study. PLoS One. 7(5):e37455, 2012. (HU, SL)

BACKGROUND: There is persistent public concern about sleep disturbances due to radiofrequency electromagnetic field (RF-EMF) exposure. The aim of this prospective cohort study was to investigate whether sleep quality is affected by mobile phone use or by other RF-EMF sources in the everyday environment. METHODS: We conducted a prospective cohort study with 955 study participants aged between 30 and 60 years. Sleep quality and daytime sleepiness was assessed by means of standardized questionnaires in May 2008 (baseline) and May 2009 (follow-up). We also asked about mobile and cordless phone use and asked study participants for consent to obtain their mobile phone connection data from the mobile phone operators. Exposure to environmental RF-EMF was computed for each study participant using a previously developed and validated prediction model. In a nested sample of 119 study participants, RF-EMF exposure was measured in the bedroom and data on sleep behavior was collected by means of actigraphy during two weeks. Data were analyzed using multivariable regression models adjusted for relevant confounders. RESULTS: In the longitudinal analyses neither operator-recorded nor self-reported mobile phone use was associated with sleep disturbances or daytime sleepiness. Also, exposure to environmental RF-EMF did not affect self-reported sleep quality. The results from the longitudinal analyses were confirmed in the nested sleep study with objectively recorded exposure and measured sleep behavior data. CONCLUSIONS: We did not find evidence for adverse effects on sleep quality from RF-EMF exposure in our everyday environment.

(E) Mohammed HS, Fahmy HM, Radwah NM, Elsayed AA. Non-thermal continuous and modulated electromagnetic radiation fields effects on sleep EEG of rats. J Adv Res 4(2) 181-187, 2013. (AS, CE, EE, SL, WS)

In the present study, the alteration in the sleep EEG in rats due to chronic exposure to low-level non-thermal electromagnetic radiation was investigated. Two types of radiation fields were used; 900 MHz *unmodulated* wave and 900 MHz *modulated* at 8 and 16 Hz waves. Animals has exposed to radiation fields for 1 month (1 h/day). EEG power spectral analyses of exposed and

control animals during slow wave sleep (SWS) and rapid eye movement sleep (REM sleep) revealed that the REM sleep is more susceptible to modulated radiofrequency radiation fields (RFR) than the SWS. The latency of REM sleep increased due to radiation exposure indicating a change in the ultradian rhythm of normal sleep cycles. The cumulative and irreversible effect of radiation exposure was proposed and the interaction of the extremely low frequency radiation with the similar EEG frequencies was suggested.

(E) Moretti D, Garenne A, Haro E, Poulletier de Gannes F, Lagroye I, Lévêque P, Veyret B, Lewis N. In-vitro exposure of neuronal networks to the GSM-1800 signal. Bioelectromagnetics. 34(8):571-578, 2013. (CS, EE)

The central nervous system is the most likely target of mobile telephony radiofrequency (RF) field exposure in terms of biological effects. Several electroencephalography (EEG) studies have reported variations in the alpha-band power spectrum during and/or after RF exposure, in resting EEG and during sleep. In this context, the observation of the spontaneous electrical activity of neuronal networks under RF exposure can be an efficient tool to detect the occurrence of low-level RF effects on the nervous system. Our research group has developed a dedicated experimental setup in the GHz range for the simultaneous exposure of neuronal networks and monitoring of electrical activity. A transverse electromagnetic (TEM) cell was used to expose the neuronal networks to GSM-1800 signals at a SAR level of 3.2 W/kg. Recording of the neuronal electrical activity and detection of the extracellular spikes and bursts under exposure were performed using microelectrode arrays (MEAs). This work provides the proof of feasibility and preliminary results of the integrated investigation regarding exposure setup, culture of the neuronal network, recording of the electrical activity, and analysis of the signals obtained under RF exposure. In this pilot study on 16 cultures, there was a 30% reversible decrease in firing rate (FR) and bursting rate (BR) during a 3 min exposure to RF. Additional experiments are needed to further characterize this effect.

(E) Mortazavi SM, Rouintan MS, Taeb S, Dehghan N, Ghaffarpanah AA, Sadeghi Z, Ghafouri F. Human short-term exposure to electromagnetic fields emitted by mobile phones decreases computer-assisted visual reaction time. Acta Neurol Belg. 112(2):171-175, 2012. (HU, BE)

The worldwide dramatic increase in mobile phone use has generated great concerns about the detrimental effects of microwave radiations emitted by these communication devices. Reaction time plays a critical role in performing tasks necessary to avoid hazards. As far as we know, this study is the first survey that reports decreased reaction time after exposure to electromagnetic fields generated by a high specific absorption rate mobile phone. It is also the first study in which previous history of mobile phone use is taken into account. The aim of this study was to assess both the acute and chronic effects of electromagnetic fields emitted by mobile phones on reaction time in university students. Visual reaction time (VRT) of young university students was recorded with a simple blind computer-assisted-VRT test, before and after a 10 min

real/sham exposure to electromagnetic fields of mobile phones. Participants were 160 right-handed university students aged 18-31. To assess the effect of chronic exposures, the reaction time in sham-exposed phases were compared among low level, moderate and frequent users of mobile phones. The mean ± SD reaction time after real exposure and sham exposure were 286.78 ± 31.35 ms and 295.86 ± 32.17 ms (P < 0.001), respectively. The age of students did not significantly alter the reaction time either in talk or in standby mode. The reaction time either in talk or in standby mode was shorter in male students. The students' VRT was significantly affected by exposure to electromagnetic fields emitted by a mobile phone. It can be concluded that these exposures cause decreased reaction time, which may lead to a better response to different hazards. In this light, this phenomenon might decrease the chances of human errors and fatal accidents.

(E) Mortazavi SM, Taeb S, Dehghan N. Alterations of visual reaction time and short term memory in military radar personnel. Iran J Public Health. 42(4):428-435, 2013. (HU, BE)

BACKGROUND: Radar transmitters emit high-power radiofrequency radiation by creation of a high-voltage and high-frequency alternating electrical current. METHODS: Health effects of occupational exposure to military radar were investigated. Visual reaction time was recorded with a simple blind computer-assisted-visual reaction time test. To assess the short-term memory, modified Wechsler Memory Scale test was performed. RESULTS: The mean +/- SD reaction time in radar works (N=100) and the control group (N=57) were 238.58 +/- 23.47 milliseconds and 291.86 +/- 28.26 milliseconds (P<0.0001), respectively. The scores of forward digit span in radar works and the control group were 3.56 +/- 0.77 and 4.29 +/- 1.06 (P<0.0001), while the scores of backward digit span in radar works and the control group were 2.70 +/- 0.69 and 3.62 +/- 0.95 (P<0.0001). The scores of word recognition in radar works and the control group were 3.37 +/- 1.13 and 5.86 +/- 1.11 (P<0.0001). Finally, the scores of paired words in radar works and the control group were 13.56 +/- 1.78 and 15.21 +/- 2.20 (P<0.0001). It can be concluded that occupational exposures to radar radiations decreases reaction time, which may lead to a better response to different hazards. CONCLUSION: To the best of our knowledge, this is the first study to show that occupational exposure to radar microwave radiation leads to decreased reaction time and the lower performance of short-term memory. Altogether, these results indicate that occupational exposure to radar microwave radiations may be linked to some non-detrimental and detrimental health effects.

(E) Motawi TK, Darwish HA, Moustafa YM, Labib MM. Biochemical Modifications and Neuronal Damage in Brain of Young and Adult Rats After Long-Term Exposure to Mobile Phone Radiations. Cell Biochem Biophys. 70:845-855, 2014. (AS, CE, CH, CC, OX)

This study investigated the effect of exposure to mobile phone radiations on oxidative stress and apoptosis in brain of rats. Rats were allocated into six groups (three young and three adult). Groups 1 and 4 were not subjected to the radiation source and served as control groups. In

groups 2 and 5, the mobile phones were only connected to the global system for mobile communication, while in groups 3 and 6, the option of calling was in use. Microwaves were generated by a mobile test phone (SAR = 1.13 W/kg) during 60 days (2 h/day). Significant increments in conjugated dienes, protein carbonyls, total oxidant status, and oxidative stress index along with a significant reduction of total antioxidant capacity levels were evident after exposure. Bax/Bcl-2 ratio, caspase-3 activity, and tumor necrosis factor-alpha level were enhanced, whereas no DNA fragmentation was detected. The relative brain weight of young rats was greatly affected, and histopathological examination reinforced the neuronal damage. The study highlights the detrimental effects of mobile phone radiations on brain during young and adult ages. The interaction of these radiations with brain is via dissipating its antioxidant status and/or triggering apoptotic cell death.

(E) Movvahedi MM, Tavakkoli-Golpayegani A, Mortazavi SA, Haghani M, Razi Z, Shojaie-Fard MB, Zare M, Mina E, Mansourabadi L, Nazari-Jahromi, Safari A, Shokrpour N, Mortazavi SM. Does exposure to GSM 900 MHz mobile phone radiation affect short-term memory of elementary school students? J Pediatr Neurosci. 9(2):121-124, 2014. (HU, BE)

BACKGROUND: Now-a-days, children are exposed to mobile phone radiation at a very early age. We have previously shown that a large proportion of children in the city of Shiraz, Iran use mobile phones. Furthermore, we have indicated that the visual reaction time (VRT) of university students was significantly affected by a 10 min real/sham exposure to electromagnetic fields emitted by mobile phone. We found that these exposures decreased the reaction time which might lead to a better response to different hazards. We have also revealed that occupational exposures to radar radiations decreased the reaction time in radar workers. The purpose of this study was to investigate whether short-term exposure of elementary school students to radiofrequency (RF) radiation leads to changes in their reaction time and short-term memory. MATERIALS AND METHODS: A total of 60 elementary school children ages ranging from 8 to 10 years studying at a public elementary school in Shiraz, Iran were enrolled in this study. Standardized computer-based tests of VRT and short-term memory (modified for children) were administered. The students were asked to perform some preliminary tests for orientation with the VRT test. After orientation, to reduce the random variation of measurements, each test was repeated ten times in both real and sham exposure phases. The time interval between the two subsequent sham and real exposure phases was 30 min. RESULTS: The mean ± standard deviation reaction times after a 10 min talk period and after a 10 min sham exposure (switched off mobile) period were 249.0 ± 82.3 ms and 252.9 ± 68.2 ms (P = 0.629), respectively. On the other hand, the mean short-term memory scores after the talk and sham exposure periods were 1062.60 ± 305.39, and 1003.84 ± 339.68 (P = 0.030), respectively. Conclusion: To the best of our knowledge, this is the first study to show that short-term exposure of elementary school students to RF radiation leads to the better performance of their short-term memory.

(E) Mugunthan N, Shanmugasamy K, Anbalagan J, Rajanarayanan S, Meenachi S. Effects of Long Term Exposure of 900-1800 MHz Radiation Emitted from 2G Mobile Phone on Mice Hippocampus- A Histomorphometric Study. J Clin Diagn Res. 10(8):AF01-6, 2016. (AS, CE, CC)

INTRODUCTION: The advancement in the telecommunications technology with multi-functional added features in mobile phone, attracts more users of all age group. It is alarming to note that, the mobile phone use has increased amongst children and they are exposed to potentially harmful radiofrequency radiation in their lifetime. AIM: To investigate the long term exposure of 900 to 1800 MHz radiations emitted from 2G mobile phone in mice hippocampus at histomorphometric level. MATERIALS AND METHODS: With due approval from institutional animal ethics committee, 36 mice were exposed to 2G mobile phone radiation, 48 minutes per day for a period of 30-180 days. The control group was kept under similar conditions without 2G exposure. Mice were sacrificed and the brain was removed from the first month to six months period. Brain was removed from the cranial cavity and hippocampus region was dissected out carefully and processed for routine histological study. Random serial sections were analysed under microscope for histomorphometric changes. For statistical analysis, independent t-test was used for comparing control and 2G exposed groups. RESULTS: The mean density of neurons in the hippocampus regions CA1, CA2 and DGDB from first to sixth month was significantly lower in the 2G exposed groups; however, in CA3 and DGVB, the 2G exposed mice showed significantly higher density of neurons. The mean nuclear diameter of neurons in the hippocampus region of CA1, CA2, CA3, DGDB and DGVB from first to sixth months showed lower nuclear diameter in 2G exposed mice. CONCLUSION: The long term exposure to 900-1800 MHz frequency radiations emitted from 2G mobile phone could cause significantly reduced neuron density and decreased nuclear diameter in the hippocampus neurons of mice.

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(NE) Nakatani-Enomoto S, Furubayashi T, Ushiyama A, Groiss SJ, Ueshima K, Sokejima S, Simba AY, Wake K, Watanabe SI, Nishikawa M, Miyawaki K, Taki M, Ugawa Y. Effects of electromagnetic fields emitted from W-CDMA-like mobile phones on sleep in humans. Bioelectromagnetics. 34:589-598, 2013. (HU, EE, SL)

In this study, we investigated subjective and objective effects of mobile phones using a Wideband Code Division Multiple Access (W-CDMA)-like system on human sleep. Subjects were 19 volunteers. Real or sham electromagnetic field (EMF) exposures for 3 h were performed before their usual sleep time on 3 consecutive days. They were exposed to real EMF on the second or third experimental day in a double-blind design. Sleepiness and sleep insufficiency were evaluated the next morning. Polysomnograms were recorded for analyses of the sleep variables and power spectra of electroencephalograms (EEG). No significant differences were observed between the two conditions in subjective feelings. Sleep parameters including sleep stage percentages and EEG power spectra did not differ significantly between real and sham exposures. We conclude that continuous wave EMF exposure for 3 h from a W-CDMA-like system has no detectable effects on human sleep.

(E) Narayanan SN, Kumar RS, Potu BK, Nayak S, Mailankot M. Spatial memory performance of Wistar rats exposed to mobile phone. Clinics (Sao Paulo). 64(3):231-234, 2009. (AS, CE, BE)

INTRODUCTION: With the tremendous increase in number of mobile phone users world wide, the possible risks of this technology have become a serious concern. OBJECTIVE: We tested the effects of mobile phone exposure on spatial memory performance. MATERIALS AND METHODS: Male Wistar rats (10-12 weeks old) were exposed to 50 missed calls/day for 4 weeks from a GSM (900/1800 MHz) mobile phone in vibratory mode (no ring tone). After the experimental period, the animals were tested for spatial memory performance using the Morris water maze test. RESULTS: Both phone exposed and control animals showed a significant decrease in escape time with training. Phone exposed animals had significantly (approximately 3 times) higher mean latency to reach the target quadrant and spent significantly (approximately 2 times) less time in the target quadrant than age- and sex-matched controls. CONCLUSION: Mobile phone exposure affected the acquisition of learned responses in Wistar rats. This in turn points to the poor spatial navigation and the object place configurations of the phone-exposed animals.

(E) Narayanan SN, Kumar RS, Potu BK, Nayak S, Bhat PG, Mailankot M. Effect of radio-frequency electromagnetic radiations (RF-EMR) on passive avoidance behaviour and hippocampal morphology in Wistar rats. Ups J Med Sci. 115(2):91-96, 2010. (AS, CE, ME, BE)

INTRODUCTION: The interaction of mobile phone radio-frequency electromagnetic radiation (RF-EMR) with the brain is a serious concern of our society. **OBJECTIVE:** We evaluated the effect of RF-EMR from mobile phones on passive avoidance behaviour and hippocampal morphology in rats. **MATERIALS AND METHODS:** Healthy male albino Wistar rats were exposed to RF-EMR by giving 50 missed calls (within 1 hour) per day for 4 weeks, keeping a GSM (0.9 GHz/1.8 GHz) mobile phone in vibratory mode (no ring tone) in the cage. After the experimental period, passive avoidance behaviour and hippocampal morphology were studied. **RESULTS:** Passive avoidance behaviour was significantly affected in mobile phone RF-EMR-exposed rats demonstrated as shorter entrance latency to the dark compartment when compared to the control rats. Marked morphological changes were also observed in the CA(3) region of the hippocampus of the mobile phone-exposed rats in comparison to the control rats. **CONCLUSION:** Mobile phone RF-EMR exposure significantly altered the passive avoidance behaviour and hippocampal morphology in rats.

(E) Narayanan SN, Kumar RS, Paval J, Kedage V, Bhat MS, Nayak S, Bhat PG. Analysis of emotionality and locomotion in radio-frequency electromagnetic radiation exposed rats. Neurol Sci. 34(7):1117-1124, 2013. (AS, CE, BE)

In the current study the modulatory role of mobile phone radio-frequency electromagnetic radiation (RF-EMR) on emotionality and locomotion was evaluated in adolescent rats. Male albino Wistar rats (6-8 weeks old) were randomly assigned into the following groups having 12 animals in each group. Group I (Control): they remained in the home cage throughout the experimental period. Group II (Sham exposed): they were exposed to mobile phone in switch-off mode for 28 days, and Group III (RF-EMR exposed): they were exposed to RF-EMR (900 MHz) from an active GSM (Global system for mobile communications) mobile phone with a peak power density of 146.60 µW/cm(2) for 28 days. On 29th day, the animals were tested for

emotionality and locomotion. Elevated plus maze (EPM) test revealed that, percentage of entries into the open arm, percentage of time spent on the open arm and distance travelled on the open arm were significantly reduced in the RF-EMR exposed rats. Rearing frequency and grooming frequency were also decreased in the RF-EMR exposed rats. Defecation boli count during the EPM test was more with the RF-EMR group. No statistically significant difference was found in total distance travelled, total arm entries, percentage of closed arm entries and parallelism index in the RF-EMR exposed rats compared to controls. Results indicate that mobile phone radiation could affect the emotionality of rats without affecting the general locomotion.

(E) Narayanan SN, Kumar RS, Kedage V, Nalini K, Nayak S, Bhat PG. Evaluation of oxidant stress and antioxidant defense in discrete brain regions of rats exposed to 900 MHz radiation. Bratisl Lek Listy. 115(5):260-266, 2014. (AS, CE, CH, OX)

AIM: In the current study, the effects of 900 MHz radio-frequency electromagnetic radiation (RF-EMR) on levels of thiobarbituric acid-reactive substances (TBARS), total antioxidants (TA), and glutathione S-transferase (GST) activity in discrete brain regions were studied in adolescent rats. MATERIALS AND METHODS: Thirty-six male Wistar rats (6-8 weeks old) were allotted into three groups (n = 12 in each group). Control group (1) remained undisturbed in their home cage; sham group (2) was exposed to mobile phone in switch off mode for four weeks; RF-EMR-exposed group (3) was exposed to 900 MHz of RF-EMR (1 hr/day with peak power density of 146.60 µW/cm2) from an activated Global System for Mobile communication (GSM) mobile phone (kept in silent mode; no ring tone and no vibration) for four weeks. On 29th day, behavioral analysis was done. Followed by this, six animals from each group were sacrificed and biochemical parameters were studied in amygdala, hippocampus, frontal cortex, and cerebellum. RESULTS: Altered behavioral performances were found in RF-EMR-exposed rats. Additionally, elevated TBARS level was found with all brain regions studied. RF-EMR exposure significantly decreased TA in the amygdala and cerebellum but its level was not significantly changed in other brain regions. GST activity was significantly decreased in the hippocampus but, its activity was unaltered in other brain regions studied. CONCLUSION: RF-EMR exposure for a month induced oxidative stress in rat brain, but its magnitude was different in different regions studied. RF-EMR-induced oxidative stress could be one of the underlying causes for the behavioral deficits seen in rats after RF-EMR exposure (Fig. 5, Ref. 37).

(E) Narayanan SN, Kumar RS, Karun KM, Nayak SB, Bhat PG. Possible cause for altered spatial cognition of prepubescent rats exposed to chronic radiofrequency electromagnetic radiation. Metab Brain Dis. 30:1193-1206, 2015. (AS, CE, BE, ME)

The effects of chronic and repeated radiofrequency electromagnetic radiation (RFEMR) exposure on spatial cognition and hippocampal architecture were investigated in prepubescent

rats. Four weeks old male Wistar rats were exposed to RF-EMR (900 MHz; SAR-1.15 W/kg with peak power density of 146.60 μW/cm^2) for 1 h/day, for 28 days. Followed by this, spatial cognition was evaluated by Morris water maze test. To evaluate the hippocampal morphology; H&E staining, cresyl violet staining, and Golgi-Cox staining were performed on hippocampal sections. CA3 pyramidal neuron morphology and surviving neuron count (in CA3 region) were studied using H&E and cresyl violet stained sections. Dendritic arborization pattern of CA3 pyramidal neuron was investigated by concentric circle method. Progressive learning abilities were found to be decreased in RF-EMR exposed rats. Memory retention test performed 24 h after the last training revealed minor spatial memory deficit in RF-EMR exposed group. However, RF-EMR exposed rats exhibited poor spatial memory retention when tested 48 h after the final trial. Hirano bodies and Granulovacuolar bodies were absent in the CA3 pyramidal neurons of different groups studied. Nevertheless, RF-EMR exposure affected the viable cell count in dorsal hippocampal CA3 region. RF-EMR exposure influenced dendritic arborization pattern of both apical and basal dendritic trees in RF-EMR exposed rats. Structural changes found in the hippocampus of RF-EMR exposed rats could be one of the possible reasons for altered cognition.

(E) Naziroğlu M, Gümral N. Modulator effects of L-carnitine and selenium on wireless devices (2.45 GHz)-induced oxidative stress and electroencephalography records in brain of rat. Int J Radiat Biol. 85(8):680-689, 2009. (AS, CE, CH, EE, OX)

PURPOSE: Electromagnetic radiation (EMR) from wireless devices may affect biological systems by increasing free radicals. The present study was designed to determine the effects of 2.45 GHz EMR on the brain antioxidant redox system and electroencephalography (EEG) records in rat. The possible protective effects of selenium and L-carnitine were also tested and compared to untreated controls. MATERIALS AND METHODS: Thirty rats were equally divided into five different groups, namely Group A(1): Cage control, Group A(2): Sham control, group B: 2.45 GHz EMR, group C: 2.45 GHz EMR + selenium, group D: 2.45 GHz EMR + L-carnitine. Groups B, C and D were exposed to 2.45 GHz EMR during 60 min/day for 28 days. End of the experiments, EEG records and the brain cortex samples were taken. RESULTS: The cortex brain vitamin A ($p < 0.05$), vitamin C ($p < 0.01$) and vitamin E ($p < 0.05$) concentrations values were lower in group B than in group A1 and A2 although their concentrations were increased by selenium and L-carnitine supplementation. Lipid peroxidation, levels were lower in group C ($p < 0.05$) and D ($p < 0.01$) than in group B where as reduced glutathione levels were higher in group C ($p < 0.05$) than in group A1, A2 and B. However, B-carotene levels did not change in the five groups. CONCLUSIONS: L-carnitine and selenium seem to have protective effects on the 2.45 GHz-induced decrease of the vitamins by supporting antioxidant redox system. L-carnitine on the vitamin concentrations seems to more protective affect than in selenium.

(E) Nazıroğlu M, Çelik Ö, Özgül C, Çiğ B, Doğan S, Bal R, Gümral N, Rodríguez AB, Pariente JA. Melatonin modulates wireless (2.45 GHz)-induced oxidative injury through TRPM2 and

voltage gated Ca(2+) channels in brain and dorsal root ganglion in rat. Physiol Behav. 105(3):683-692, 2012. (AS, CE, CH, EE, OX)

We aimed to investigate the protective effects of melatonin and 2.45 GHz electromagnetic radiation (EMR) on brain and dorsal root ganglion (DRG) neuron antioxidant redox system, Ca(2+) influx, cell viability and electroencephalography (EEG) records in the rat. Thirty two rats were equally divided into four different groups namely group A1: Cage control, group A2: Sham control, group B: 2.45 GHz EMR, group C: 2.45 GHz EMR+melatonin. Groups B and C were exposed to 2.45 GHz EMR during 60 min/day for 30 days. End of the experiments, EEG records and the brain cortex and DRG samples were taken. Lipid peroxidation (LP), cell viability and cytosolic Ca(2+) values in DRG neurons were higher in group B than in groups A1 and A2 although their concentrations were increased by melatonin, 2-aminoethyldiphenyl borinate (2-APB), diltiazem and verapamil supplementation. Spike numbers of EEG records in group C were lower than in group B. Brain cortex vitamin E concentration was higher in group C than in group B. In conclusion, Melatonin supplementation in DRG neurons and brain seems to have protective effects on the 2.45 GHz-induced increase Ca(2+) influx, EEG records and cell viability of the hormone through TRPM2 and voltage gated Ca(2+) channels.

(NE) Nazıroğlu M, Ozkan FF, Hapil SR, Ghazizadeh V, Ciğ B. Epilepsy But Not Mobile Phone Frequency (900 MHz) Induces Apoptosis and Calcium Entry in Hippocampus of Epileptic Rat: Involvement of TRPV1 Channels. J Membr Biol. 248:83-91, 2015.] (CS, CC, IA)

Electromagnetic radiation (EMR) and epilepsy are reported to mediate the regulation of apoptosis and oxidative stress through Ca^{2+} influx. Results of recent reports indicated that EMR can increase temperature and oxidative stress of body cells, and TRPV1 channel is activated by noxious heat, oxidative stress, and capsaicin (CAP). We investigated the effects of mobile phone (900 MHz) EMR exposure on Ca^{2+} influx, apoptosis, oxidative stress, and TRPV1 channel activations in the hippocampus of pentylenetetrazol (PTZ)-induced epileptic rats. Freshly isolated hippocampal neurons of twenty-one rats were used in study within three groups namely control, PTZ, and PTZ + EMR. The neurons in the three groups were stimulated by CAP. Epilepsy was induced by PTZ administration. The neurons in PTZ + EMR group were exposed to the 900 MHz EMR for 1 h. The apoptosis, mitochondrial membrane depolarization, intracellular reactive oxygen species (ROS), and caspase-3 and caspase-9 values were higher in PTZ and PTZ + EMR groups than in control. However, EMR did not add additional increase effects on the values in the hippocampal neurons. Intracellular-free Ca^{2+} concentrations in fura-2 analyses were also higher in PTZ + CAP group than in control although their concentrations were decreased by TRPV1 channel blocker, capsazepine. However, there were no statistical changes on the Ca^{2+} concentrations between epilepsy and EMR groups. In conclusion, apoptosis, mitochondrial, ROS, and Ca^{2+} influx via TRPV1 channel were increased in the hippocampal neurons by epilepsy induction although the mobile phone did not change the values. The results indicated that TRPV1 channels in hippocampus may possibly be a novel target for effective target of epilepsy.

(E) Ning W, Xu SJ, Chiang H, Xu ZP, Zhou SY, Yang W, Luo JH. Effects of GSM 1800 MHz on dendritic development of cultured hippocampal neurons. Acta Pharmacol Sin. 28(12):1873-1880, 2007. (CS, CE, DE, ME)

AIM: To evaluate the effects of global system for mobile communications (GSM) 1800 MHz microwaves on dendritic filopodia, dendritic arborization, and spine maturation during development in cultured hippocampal neurons in rats. **METHODS:** The cultured hippocampal neurons were exposed to GSM 1800 MHz microwaves with 2.4 and 0.8 W/kg, respectively, for 15 min each day from 6 days in vitro (DIV6) to DIV14. The subtle structures of dendrites were displayed by transfection with farnesylated enhanced green fluorescent protein (F-GFP) and GFP-actin on DIV5 into the hippocampal neurons. **RESULTS:** There was a significant decrease in the density and mobility of dendritic filopodia at DIV8 and in the density of mature spines at DIV14 in the neurons exposed to GSM 1800 MHz microwaves with 2.4 W/kg. In addition, the average length of dendrites per neuron at DIV10 and DIV14 was decreased, while the dendritic arborization was unaltered in these neurons. However, there were no significant changes found in the neurons exposed to the GSM 1800 MHz microwaves with 0.8 W/kg. **CONCLUSION:** These data indicate that the chronic exposure to 2.4 W/kg GSM 1800 MHz microwaves during the early developmental stage may affect dendritic development and the formation of excitatory synapses of hippocampal neurons in culture.

(E) Nirwane A, Sridhar V, Majumdar A. Neurobehavioural Changes and Brain Oxidative Stress Induced by Acute Exposure to GSM 900 Mobile Phone Radiations in Zebrafish (Danio rerio). Toxicol Res. 32(2):123-132, 2016. (AS, CE, BE, OX)

The impact of mobile phone (MP) radiation on the brain is of specific interest to the scientific community and warrants investigations, as MP is held close to the head. Studies on humans and rodents revealed hazards MP radiation associated such as brain tumors, impairment in cognition, hearing etc. Melatonin (MT) is an important modulator of CNS functioning and is a neural antioxidant hormone. Zebrafish has emerged as a popular model organism for CNS studies. Herein, we evaluated the impact of GSM900MP (GSM900MP) radiation exposure daily for 1 hr for 14 days with the SAR of 1.34W/Kg on neurobehavioral and oxidative stress parameters in zebrafish. Our study revealed that, GSM900MP radiation exposure, significantly decreased time spent near social stimulus zone and increased total distance travelled, in social interaction test. In the novel tank dive test, the GSM900MP radiation exposure elicited anxiety as revealed by significantly increased time spent in bottom half; freezing bouts and duration and decreased distance travelled, average velocity, and number of entries to upper half of the tank. Exposed zebrafish spent less time in the novel arm of the Y-Maze, corroborating significant impairment in learning as compared to the control group. Exposure decreased superoxide dismutase (SOD), catalase (CAT) activities whereas, increased levels of reduced glutathione (GSH) and lipid peroxidation (LPO) was encountered showing compromised antioxidant defense. Treatment with MT significantly reversed the above neurobehavioral and oxidative derangements induced by GSM900MP radiation exposure. This study traced GSM900MP radiation exposure induced neurobehavioral aberrations and alterations in brain

oxidative status. Furthermore, MT proved to be a promising therapeutic candidate in ameliorating such outcomes in zebrafish.

(E) Nittby H, Widegren B, Krogh M, Grafström G, Berlin H, Rehn G, Eberhardt JL, Malmgren L, Persson BRR, Salford L. Exposure to radiation from global system for mobile communications at 1,800 MHz significantly changes gene expression in rat hippocampus and cortex. Environmentalist 28(4), 458-465, 2008. (AS, CH, LI)

We have earlier shown that radio frequency electromagnetic fields can cause significant leakage of albumin through the blood–brain barrier of exposed rats as compared to non-exposed rats, and also significant neuronal damage in rat brains several weeks after a 2 h exposure to a mobile phone, at 915 MHz with a global system for mobile communications (GSM) frequency modulation, at whole-body specific absorption rate values (SAR) of 200, 20, 2, and 0.2 mW/kg. We have now studied whether 6 h of exposure to the radiation from a GSM mobile test phone at 1,800 MHz (at a whole-body SAR-value of 13 mW/kg, corresponding to a brain SAR-value of 30 mW/kg) has an effect upon the gene expression pattern in rat brain cortex and hippocampus—areas where we have observed albumin leakage from capillaries into neurons and neuronal damage. Microarray analysis of 31,099 rat genes, including splicing variants, was performed in cortex and hippocampus of 8 Fischer 344 rats, 4 animals exposed to global system for mobile communications electromagnetic fields for 6 h in an anechoic chamber, one rat at a time, and 4 controls kept as long in the same anechoic chamber without exposure, also in this case one rat at a time. Gene ontology analysis (using the gene ontology categories biological processes, molecular functions, and cell components) of the differentially expressed genes of the exposed animals versus the control group revealed the following highly significant altered gene categories in both cortex and hippocampus: extracellular region, signal transducer activity, intrinsic to membrane, and integral to membrane. The fact that most of these categories are connected with membrane functions may have a relation to our earlier observation of albumin transport through brain capillaries.

(E) Nittby H, Grafström G, Tian DP, Malmgren L, Brun A, Persson BR, Salford LG, Eberhardt J. Cognitive impairment in rats after long-term exposure to GSM-900 mobile phone radiation. Bioelectromagnetics. 29(3):219-232, 2008. (AS, CE, BE, LI)

Considering the frequent use of mobile phones, we have directed attention to possible implications on cognitive functions. In this study we investigated in a rat model the long-term effects of protracted exposure to Global System for Mobile Communication-900 MHz (GSM-900) radiation. Out of a total of 56 rats, 32 were exposed for 2 h each week for 55 weeks to radio-frequency electromagnetic radiation at different SAR levels (0.6 and 60 mW/kg at the initiation of the experimental period) emitted by a (GSM-900) test phone. Sixteen animals were sham exposed and eight animals were cage controls, which never left the animal house. After this protracted exposure, GSM-900 exposed rats were compared to sham exposed controls. Effects on exploratory behaviour were evaluated in the open-field test, in which no difference was seen. Effects on cognitive functions were evaluated in the episodic-like memory test. In our study, GSM exposed rats had impaired memory for objects and their temporal order of

presentation, compared to sham exposed controls (P = 0.02). Detecting the place in which an object was presented was not affected by GSM exposure. Our results suggest significantly reduced memory functions in rats after GSM microwave exposure (P = 0.02).

(E) Nittby H, Brun A, Eberhardt J, Malmgren L, Persson BR, Salford LG. Increased blood-brain barrier permeability in mammalian brain 7 days after exposure to the radiation from a GSM-900 mobile phone. Pathophysiology. 16(2-3):103-112, 2009. (AS, ME, LI)

Microwaves were for the first time produced by humans in 1886 when radio waves were broadcasted and received. Until then microwaves had only existed as a part of the cosmic background radiation since the birth of universe. By the following utilization of microwaves in telegraph communication, radars, television and above all, in the modern mobile phone technology, mankind is today exposed to microwaves at a level up to 10(20) times the original background radiation since the birth of universe. Our group has earlier shown that the electromagnetic radiation emitted by mobile phones alters the permeability of the blood-brain barrier (BBB), resulting in albumin extravasation immediately and 14 days after 2h of exposure. In the background section of this report, we present a thorough review of the literature on the demonstrated effects (or lack of effects) of microwave exposure upon the BBB. Furthermore, we have continued our own studies by investigating the effects of GSM mobile phone radiation upon the blood-brain barrier permeability of rats 7 days after one occasion of 2h of exposure. Forty-eight rats were exposed in TEM-cells for 2h at non-thermal specific absorption rates (SARs) of 0mW/kg, 0.12mW/kg, 1.2mW/kg, 12mW/kg and 120mW/kg. Albumin extravasation over the BBB, neuronal albumin uptake and neuronal damage were assessed. Albumin extravasation was enhanced in the mobile phone exposed rats as compared to sham controls after this 7-day recovery period (Fisher's exact probability test, p=0.04 and Kruskal-Wallis, p=0.012), at the SAR-value of 12mW/kg (Mann-Whitney, p=0.007) and with a trend of increased albumin extravasation also at the SAR-values of 0.12mW/kg and 120mW/kg. There was a low, but significant correlation between the exposure level (SAR-value) and occurrence of focal albumin extravasation (r(s)=0.33; p=0.04). The present findings are in agreement with our earlier studies where we have seen increased BBB permeability immediately and 14 days after exposure. We here discuss the present findings as well as the previous results of altered BBB permeability from our and other laboratories.

(E) Nittby H, Moghadam MK, Sun W, Malmgren L, Eberhardt J, Persson BR, Salford LG. Analgetic effects of non-thermal GSM-1900 radiofrequency electromagnetic fields in the land snail Helix pomatia. Int J Radiat Biol. 88(3):245-252, 2012. (AS, BE, MA, LI)

PURPOSE: To investigate whether mobile phone radiation might affect snail nociception, employing radiofrequency (RF) electromagnetic fields (EMF) which, to our knowledge, have hitherto not been studied in a snail model. Exposure to extremely low frequency (ELF) magnetic fields has however been shown to significantly affect nociceptive responses. MATERIALS AND METHODS: In the present study, we exposed 29 land snails of the strain Helix pomatia to global system for mobile communications (GSM) EMF at 1900 MHz at the non-thermal level 48 mW/kg for 1 hour each and 29 snails were sham controls. The experiments took place during

the onset of summer, with all snails being well out of hibernation. Before and after GSM or sham exposure, the snails were subjected to thermal pain by being placed on a hot plate. The reaction time for retraction from the hot plate was measured by two blinded observers. RESULTS: Comparing the reaction pattern of each snail before and after exposure, the GSM-exposed snails were less sensitive to thermal pain as compared to the sham controls, indicating that RF exposure induces a significant analgesia (Mann-Whitney $p < 0.001$). CONCLUSION: This study might support earlier findings, describing beneficial effects of EMF exposure upon nociception.

(E) Noor NA, Mohammed HS, Ahmed NA, Radwan NM. Variations in amino acid neurotransmitters in some brain areas of adult and young male albino rats due to exposure to mobile phone radiation. Eur Rev Med Pharmacol Sci. 15(7):729-742, 2011. (AS, CE, CH, AD)

BACKGROUND AND OBJECTIVES: Mobile phone radiation and health concerns have been raised, especially following the enormous increase in the use of wireless mobile telephony throughout the world. The present study aims to investigate the effect of one hour daily exposure to electromagnetic radiation (EMR) with frequency of 900 Mz (SAR 1.165 w/kg, power density 0.02 mW/cm2) on the levels of amino acid neurotransmitters in the midbrain, cerebellum and medulla of adult and young male albino rats. **MATERIALS AND METHODS:** Adult and young rats were divided into two main groups (treated and control). The treated group of both adult and young rats was exposed to EMR for 1 hour daily. The other group of both adult and young animals was served as control. The determination of amino acid levels was carried out after 1 hour, 1 month, 2 months and 4 months of EMR exposure as well as after stopping radiation. **RESULTS:** Data of the present study showed a significant increase in both excitatory and inhibitory amino acids in the cerebellum of adult and young rats and midbrain of adult animals after 1 hour of EMR exposure. In the midbrain of adult animals, there was a significant increase in glycine level after 1 month followed by significant increase in GABA after 4 months. Young rats showed significant decreases in the midbrain excitatory amino acids. In the medulla, the equilibrium ratio percent (ER%) calculations showed a state of neurochemical inhibition after 4 months in case of adult animals, whereas in young animals, the neurochemical inhibitory state was observed after 1 month of exposure due to significant decrease in glutamate and aspartate levels. This state was converted to excitation after 4 months due to the increase in glutamate level. **CONCLUSION:** The present changes in amino acid concentrations may underlie the reported adverse effects of using mobile phones.

(E) Ntzouni MP, Stamatakis A, Stylianopoulou F, Margaritis LH. Short-term memory in mice is affected by mobile phone radiation. Pathophysiology. 18(3):193-199, 2011. (AS, CE, BE)

The effects of mobile phone electromagnetic fields (EMFs) were studied on a non-spatial memory task (Object Recognition Task - ORT) that requires entorhinal cortex function. The task was applied to three groups of mice Mus musculus C57BL/6 (exposed, sham-exposed and control) combined with 3 different radiation exposure protocols. In the first protocol designated "acute exposure", mice 45 days old (PND45 - postnatal day 45) were exposed to mobile phone (MP) radiation (SAR value 0.22W/kg) during the habituation, the training and the

test sessions of the ORT, but not during the 10min inter-trial interval (ITI) where consolidation of stored object information takes place. On the second protocol designated "chronic exposure-I", the same mice were exposed for 17 days for 90min/per day starting at PND55 to the same MP radiation. ORT recognition memory was performed at PND72 with radiation present only during the ITI phase. In the third protocol designated "chronic exposure-II", mice continued to be exposed daily under the same conditions up to PND86 having received radiation for 31 days. One day later the ORT test was performed without irradiation present in any of the sessions. The ORT-derived discrimination indices in all three exposure protocols revealed a major effect on the "chronic exposure-I" suggesting a possible severe interaction of EMF with the consolidation phase of recognition memory processes. This may imply that the primary EMF target may be the information transfer pathway connecting the entorhinal-parahippocampal regions which participate in the ORT memory task.

(E) Ntzouni MP, Skouroliakou A, Kostomitsopoulos N, Margaritis LH. Transient and cumulative memory impairments induced by GSM 1.8 GHz cell phone signal in a mouse model. Electromagn Biol Med. 32:95-102, 2013. (AS, CE, BE)

This study was designed to investigate the transient and cumulative impairments in spatial and non-spatial memory of C57Bl/6J mice exposed to GSM 1.8 GHz signal for 90 min daily by a typical cellular (mobile) phone at a specific absorption rate value of 0.11 W/kg. Free-moving male mice 2 months old were irradiated in two experimental protocols, lasting for 66 and for 148 days respectively. Each protocol used three groups of animals (n = 8 each for exposed, sham exposed and controls) in combination with two behavioural paradigms, the object recognition task and the object location task sequentially applied at different time points. One-way analysis of variance revealed statistically significant impairments of both types of memory gradually accumulating, with more pronounced effects on the spatial memory. The impairments persisted even 2 weeks after interruption of the 8 weeks daily exposure, whereas the memory of mice as detected by both tasks showed a full recovery approximately 1 month later. Intermittent every other day exposure for 1 month had no effect on both types of memory. The data suggest that visual information processing mechanisms in hippocampus, perirhinal and entorhinal cortex are gradually malfunctioning upon long-term daily exposure, a phenotype that persists for at least 2 weeks after interruption of radiation, returning to normal memory performance levels 4 weeks later. It is postulated that cellular repair mechanisms are operating to eliminate the memory affecting molecules. The overall contribution of several possible mechanisms to the observed cumulative and transient impairments in spatial and non-spatial memory is discussed.

(NE) Nylund R, Kuster N, Leszczynski D. Analysis of proteome response to the mobile phone radiation in two types of human primary endothelial cells. Proteome Sci. 8:52, 2010. (CS, CH, WS)

BACKGROUND: Use of mobile phones has widely increased over the past decade. However, in spite of the extensive research, the question of potential health effects of the mobile phone radiation remains unanswered. We have earlier proposed, and applied, proteomics as a tool to

study biological effects of the mobile phone radiation, using as a model human endothelial cell line EA.hy926. Exposure of EA.hy926 cells to 900 MHz GSM radiation has caused statistically significant changes in expression of numerous proteins. However, exposure of EA.hy926 cells to 1800 MHz GSM signal had only very small effect on cell proteome, as compared with 900 MHz GSM exposure. In the present study, using as model human primary endothelial cells, we have examined whether exposure to 1800 MHz GSM mobile phone radiation can affect cell proteome. **RESULTS:** Primary human umbilical vein endothelial cells and primary human brain microvascular endothelial cells were exposed for 1 hour to 1800 MHz GSM mobile phone radiation at an average specific absorption rate of 2.0 W/kg. The cells were harvested immediately after the exposure and the protein expression patterns of the sham-exposed and radiation-exposed cells were examined using two dimensional difference gel electrophoresis-based proteomics (2DE-DIGE). There were observed numerous differences between the proteomes of human umbilical vein endothelial cells and human brain microvascular endothelial cells (both sham-exposed). These differences are most likely representing physiological differences between endothelia in different vascular beds. However, the exposure of both types of primary endothelial cells to mobile phone radiation did not cause any statistically significant changes in protein expression. **CONCLUSIONS:** Exposure of primary human endothelial cells to the mobile phone radiation, 1800 MHz GSM signal for 1 hour at an average specific absorption rate of 2.0 W/kg, does not affect protein expression, when the proteomes were examined immediately after the end of the exposure and when the false discovery rate correction was applied to analysis. This observation agrees with our earlier study showing that the 1800 MHz GSM radiation exposure had only very limited effect on the proteome of human endothelial cell line EA.hy926, as compared with the effect of 900 MHz GSM radiation.

(NE) O'Connor RP, Madison SD, Leveque P, Roderick HL, Bootman MD. Exposure to GSM RF fields does not affect calcium homeostasis in human endothelial cells, rat pheocromocytoma cells or rat hippocampal neurons. PLoS One. 5(7):e11828, 2010. (CS, CC, CH)

In the course of modern daily life, individuals are exposed to numerous sources of electromagnetic radiation that are not present in the natural environment. The strength of the electromagnetic fields from sources such as hairdryers, computer display units and other electrical devices is modest. However, in many home and office environments, individuals can experience perpetual exposure to an "electromagnetic smog", with occasional peaks of relatively high electromagnetic field intensity. This has led to concerns that such radiation can affect health. In particular, emissions from mobile phones or mobile phone masts have been invoked as a potential source of pathological electromagnetic radiation. Previous reports have suggested that cellular calcium (Ca2+) homeostasis is affected by the types of radiofrequency fields emitted by mobile phones. In the present study, we used a high-throughput imaging platform to monitor putative changes in cellular Ca2+ during exposure of cells to 900 MHz GSM fields of differing power (specific absorption rate 0.012-2 W/Kg), thus mimicking the type of radiation emitted by current mobile phone handsets. Data from cells experiencing the 900 Mhz GSM fields were compared with data obtained from paired experiments using continuous wave fields or no field. We employed three cell types (human endothelial cells, PC-12 neuroblastoma

and primary hippocampal neurons) that have previously been suggested to be sensitive to radiofrequency fields. Experiments were designed to examine putative effects of radiofrequency fields on resting Ca2+, in addition to Ca2+ signals evoked by an InsP(3)-generating agonist. Furthermore, we examined putative effects of radiofrequency field exposure on Ca2+ store emptying and store-operated Ca2+ entry following application of the Ca2+ATPase inhibitor thapsigargin. Multiple parameters (e.g., peak amplitude, integrated Ca2+ signal, recovery rates) were analysed to explore potential impact of radiofrequency field exposure on Ca2+ signals. Our data indicate that 900 MHz GSM fields do not affect either basal Ca2+ homeostasis or provoked Ca2+ signals. Even at the highest field strengths applied, which exceed typical phone exposure levels, we did not observe any changes in cellular Ca2+ signals. We conclude that under the conditions employed in our experiments, and using a highly-sensitive assay, we could not detect any consequence of RF exposure.

(E) Odaci E, Bas O, Kaplan S. Effects of prenatal exposure to a 900 MHz electromagnetic field on the dentate gyrus of rats: a stereological and histopathological study. Brain Res. 1238:224-229, 2008. (AS, CE, DE, ME)

Electromagnetic fields (EMFs) inhibit the formation and differentiation of neural stem cells during embryonic development. In this study, the effects of prenatal exposure to EMF on the number of granule cells in the dentate gyrus of 4-week-old rats were investigated. This experiment used a control (Cont) group and an EMF exposed (EMF) group (three pregnant rats each group). The EMF group consisted of six offspring (n=6) of pregnant rats that were exposed to an EMF of up to 900 megahertz (MHz) for 60 min/day between the first and last days of gestation. The control group consisted of five offspring (n=5) of pregnant rats that were not treated at all. The offspring were sacrificed when they were 4 weeks old. The numbers of granule cells in the dentate gyrus were analyzed using the optical fractionator technique. The results showed that prenatal EMF exposure caused a decrease in the number of granule cells in the dentate gyrus of the rats ($P<0.01$). This suggests that prenatal exposure to a 900 MHz EMF affects the development of the dentate gyrus granule cells in the rat hippocampus. Cell loss might be caused by an inhibition of granule cell neurogenesis in the dentate gyrus.

(E) Odacı E, İkinci A, Yıldırım M, Kaya H, Akça M, Hancı H, Sönmez OF, Aslan A, Okuyan M, Baş O. The Effects of 900 Megahertz Electromagnetic Field Applied in the Prenatal Period on Spinal Cord Morphology and Motor Behavior in Female Rat Pups. NeuroQuantology 11:573-581, 2013. (AS, CE, DE, BE, ME)

This study investigated the effect of a 900 megahertz (MHz) electromagnetic field (EMF) applied in the prenatal period on the spinal cord and motor behavior of female rat pups. Beginning of the study, female Sprague Dawley rats (180–250 g) were left to mate with male rats. Rats identified as pregnant were then divided into control (n=3) and EMF groups (n=3). The EMF group was exposed to 1-h 900 MHz EMF daily between days 13 and 21 of pregnancy. At 21 days old, rat pups were removed from their mothers and divided into two newborn rat groups, control (n=13) and EMF (n=10). The rotarod test was applied to the rat pups to assess motor

functions and the open field test to evaluate locomotor activity. On day 32 of the study, the rat pups were decapitated, and the spinal cord in the upper thoracic region was removed. Following routine histological tests, they were stained with Cresyl fast violet. Rotarod test results revealed a significant increase in EMF group rat pups' motor functions (p=0.037). However, no difference was observed in the open field test results (p>0.05). In the EMF group' rat pups, we observed pathological changes in the spinal cord. On the basis of our results, 900 MHz EMF applied in the prenatal period affected spinal cord development. This effect was observed in the form of pathological changes in the spinal cord of rat pups, and it may be that these pathological changes led to an increase in rat pups' motor activities.

(E) Odacı E, Hancı H, İkinci A, Sönmez OF, Aslan A, Şahin A, Kaya H, Çolakoğlu S, Baş O. Maternal exposure to a continuous 900-MHz electromagnetic field provokes neuronal loss and pathological changes in cerebellum of 32-day-old female rat offspring. J Chem Neuroanat. 75(Pt B):105-110, 2016. (AS, CE, ME)

Large numbers of people are unknowingly exposed to electromagnetic fields (EMF) from wireless devices. Evidence exists for altered cerebellar development in association with prenatal exposure to EMF. However, insufficient information is still available regarding the effects of exposure to 900 megahertz (MHz) EMF during the prenatal period on subsequent postnatal cerebellar development. This study was planned to investigate the 32-day-old female rat pup cerebellum following exposure to 900MHz EMF during the prenatal period using stereological and histopathological evaluation methods. Pregnant rats were divided into control, sham and EMF groups. Pregnant EMF group (PEMFG) rats were exposed to 900MHz EMF for 1h inside an EMF cage during days 13-21 of pregnancy. Pregnant sham group (PSG) rats were also placed inside the EMF cage during days 13-21 of pregnancy for 1h, but were not exposed to any EMF. No procedure was performed on the pregnant control group (PCG) rats. Newborn control group (CG) rats were obtained from the PCG mothers, newborn sham group (SG) rats from the PSG and newborn EMF group (EMFG) rats from the PEMFG rats. The cerebellums of the newborn female rats were extracted on postnatal day 32. The number of Purkinje cells was estimated stereologically, and histopathological evaluations were also performed on cerebellar sections. Total Purkinje cell numbers calculated using stereological analysis were significantly lower in EMFG compared to CG ($p<0.05$) and SG ($p<0.05$). Additionally, some pathological changes such as pyknotic neurons with dark cytoplasm were observed in EMFG sections under light microscopy. In conclusion, our study results show that prenatal exposure to EMF affects the development of Purkinje cells in the female rat cerebellum and that the consequences of this pathological effect persist after the postnatal period.

(NE) Ogawa K, Nabae K, Wang J, Wake K, Watanabe S, Kawabe M, Fujiwara O, Takahashi S, Ichihara T, Tamano S, Shirai T. Effects of gestational exposure to 1.95-GHz W-CDMA signals for IMT-2000 cellular phones: Lack of embryotoxicity and teratogenicity in rats. Bioelectromagnetics. 30(3):205-212, 2009. (AS, CE, DE)

The present study was designed to evaluate whether gestational exposure to an EMF targeting the head region, similar to that from cellular phones, might affect embryogenesis in rats. A 1.95-GHz wide-band code division multiple access (W-CDMA) signal, which is one applied for the International Mobile Telecommunication 2000 (IMT-2000) system and used for the freedom of mobile multimedia access (FOMA), was employed for exposure to the heads of four groups of pregnant CD(SD) IGS rats (20 per group) for gestational days 7-17. The exposure was performed for 90 min/day in the morning. The spatial average specific absorption rate (SAR) for individual brains was designed to be 0.67 and 2.0 W/kg with peak brain SARs of 3.1 and 7.0 W/kg for low (group 3) and high (group 4) exposures, respectively, and a whole-body average SAR less than 0.4 W/kg so as not to cause thermal effects due to temperature elevation. Control and sham exposure groups were also included. At gestational day 20, all dams were killed and fetuses were taken out by cesarean section. There were no differences in maternal body weight gain. No adverse effects of EMF exposure were observed on any reproductive and embryotoxic parameters such as number of live (243-271 fetuses), dead or resorbed embryos, placental weights, sex ratios, weights or external, visceral or skeletal abnormalities of live fetuses.

(NE) Okano T, Terao Y, Furubayashi T, Yugeta A, Hanajima R, Ugawa Y. The effect of electromagnetic field emitted by a mobile phone on the inhibitory control of saccades. Clin Neurophysiol. 121(4):603-611, 2010. (HU, PE)

OBJECTIVE: To investigate whether exposure to a pulsed high-frequency electromagnetic field (pulsed EMF) emitted by a mobile phone has short-term effects on the inhibitory control of saccades. METHODS: A double-blind, counterbalanced crossover study design was employed. We assessed the performance of 10 normal subjects on antisaccade (AS) and cued saccade (CUED) tasks as well as two types of overlap saccade (OL1, OL2) task before and after 30 min of exposure to EMF emitted by a mobile phone or sham exposure. RESULTS: After EMF or sham exposure, we observed a slight but significant shortening of latency in the CUED and OL2 tasks. AS amplitude decreased as well as the saccade velocities in the AS, CUED, and OL1 tasks after exposure. These changes occurred regardless of whether exposure was real or sham. The frequencies of pro-saccades in the AS task, saccades to cue in the CUED task, and prematurely initiated saccades in the overlap (OL2) task did not change significantly after real or sham EMF exposure. CONCLUSIONS: Thirty minutes of mobile phone exposure has no significant short-term effect on the inhibitory control of saccades. SIGNIFICANCE: The cortical processing responsible for saccade inhibition is not affected by exposure to EMF emitted by a mobile phone.

(E) Othman H, Ammari M, Sakly M, Abdelmelek H. Effects of prenatal exposure to WIFI signal (2.45GHz) on postnatal development and behavior in rat: Influence of maternal restraint. Behav Brain Res. 326:291-302, 2017. (AS, CE, DE, BE, OX)

The present study was carried out to investigate the potential combined influence of maternal restraint stress and 2.45GHz WiFi signal exposure on postnatal development and behavior in the offspring of exposed rats. 24 pregnant albino Wistar rats were randomly assigned to four groups:

Control, WiFi-exposed, restrained and both WiFi-exposed and restrained groups. Each of WiFi exposure and restraint occurred 2h/day along gestation till parturition. The pups were evaluated for physical development and neuromotor maturation. Moreover, elevated plus maze test, open field activity and stationary beam test were also determined on postnatal days 28, 30 and 31, respectively. After behavioral tests, the rats were anesthetized and their brains were removed for biochemical analysis. Our main findings showed no detrimental effects on gestation progress and outcomes at delivery in all groups. Subsequently, WiFi and restraint, per se and mainly in concert altered physical development of pups with slight differences between genders. Behaviorally, the gestational WiFi irradiation, restraint and especially the associated treatment affected the neuromotor maturation mainly in male progeny. At adult age, we noticed anxiety, motor deficit and exploratory behavior impairment in male offspring co-exposed to WiFi radiation and restraint, and in female progeny subjected to three treatments. The biochemical investigation showed that, all three treatments produced global oxidative stress in brain of both sexes. As for serum biochemistry, phosphorus, magnesium, glucose, triglycerides and calcium levels were disrupted. Taken together, prenatal WiFi radiation and restraint, alone and combined, provoked several behavioral and biochemical impairments at both juvenile and adult age of the offspring.

(E) Özgür A, Tümkaya L, Terzi S, Kalkan Y, Erdivanlı ÖÇ, Dursun E. Effects of chronic exposure to electromagnetic waves on the auditory system. Acta Otolaryngol. 135:765-770, 2015. (AS, CE, ME)

OBJECTIVES: Numerous researches have been done about the risks of exposure to the electromagnetic fields that occur during the use of these devices, especially the effects on hearing. The aim of this study is to evaluate the effects of the electromagnetic waves emitted by the mobile phones through the electrophysiological and histological methods. METHODS: Twelve adult Wistar albino rats were included in the study. The rats were divided into two groups of six rats. The study group was exposed to the electromagnetic waves over a period of 30 days. The control group was not given any exposure to the electromagnetic fields. After the completion of the electromagnetic wave application, the auditory brainstem responses of both groups were recorded under anesthesia. The degeneration of cochlear nuclei was graded by two different histologists, both of whom were blinded to group information. RESULTS: The histopathologic and immunohistochemical analysis showed neuronal degeneration signs, such as increased vacuolization in the cochlear nucleus, pyknotic cell appearance, and edema in the group exposed to the electromagnetic fields compared to the control group. The average latency of wave in the ABR was similar in both groups ($p > 0.05$). CONCLUSION: The results support that chronic electromagnetic field exposure may cause damage by leading to neuronal degeneration of the auditory system.

(E) Pakhomov A, Bojarinova J, Cherbunin R, Chetverikova R, Grigoryev PS, Kavokin K, Kobylkov D, Lubkovskaja R, Chernetsov N. Very weak oscillating magnetic field disrupts the

magnetic compass of songbird migrants. J R Soc Interface. 2017 Aug;14(133). pii: 20170364. doi: 10.1098/rsif.2017.0364. (AS, LI, BE)

Previously, it has been shown that long-distance migrants, garden warblers (*Sylvia borin*), were disoriented in the presence of narrow-band oscillating magnetic field (1.403 MHz OMF, 190 nT) during autumn migration. This agrees with the data of previous experiments with European robins (*Erithacus rubecula*). In this study, we report the results of experiments with garden warblers tested under a 1.403 MHz OMF with various amplitudes (~0.4, 1, ~2.4, 7 and 20 nT). We found that the ability of garden warblers to orient in round arenas using the magnetic compass could be disrupted by a very weak oscillating field, such as an approximate 2.4, 7 and 20 nT OMF, but not by an OMF with an approximate 0.4 nT amplitude. The results of the present study indicate that the sensitivity threshold of the magnetic compass to the OMF lies around 2-3 nT, while in experiments with European robins the birds were disoriented in a 15 nT OMF but could choose the appropriate migratory direction when a 5 nT OMF was added to the stationary magnetic field. The radical-pair model, one of the mainstream theories of avian magnetoreception, cannot explain the sensitivity to such a low-intensity OMF, and therefore, it needs further refinement.

(E) Panda NK, Jain R, Bakshi J, Munjal S. Audiologic disturbances in long-term mobile phone users. J Otolaryngol Head Neck Surg. 39(1):5-11, 2010. (HU, CE, PE)

INTRODUCTION: There is general concern regarding the possible hazardous health effects of exposure to radiofrequency electromagnetic radiation emitted from mobile phones. This study aimed to assess the effects of chronic exposure to electromagnetic waves emitted from Global System for Mobile Communication (GSM) mobile phones on auditory functions. **MATERIAL AND METHODS:** A retrospective, cross-sectional, randomized, case control study was carried out in a tertiary care hospital. One hundred twelve subjects who were long-term mobile phone users (more than 1 year) and 50 controls who had never used a mobile phone underwent a battery of audiologic investigations including pure-tone audiometry (both speech and high frequency), tympanometry, distortion product otoacoustic emissions, auditory brain responses, and middle latency responses. Changes in the various parameters were studied in the mobile phone- and non-mobile phone-using ears of subjects and corresponding ears of the controls to ascertain the effects of electromagnetic exposure. **RESULTS:** There was no significant difference between users and controls for any of the audiologic parameters. However, trends for audiologic abnormalities were seen within the users. High-frequency loss and absent distortion product otoacoustic emissions were observed with an increase in the duration of mobile phone use, excessive use of mobile phones, and age more than 30 years. Additionally, users with some complaints during mobile phone use demonstrated absent distortion product otoacoustic emissions and abnormalities in auditory brainstem response. **CONCLUSION:** Long-term and intensive mobile phone use may cause inner ear damage. A large sample size would be required to reach definitive conclusions.

(E) Panda NK, Modi R, Munjal S, Virk RS. Auditory changes in mobile users: is evidence forthcoming? Otolaryngol Head Neck Surg. 144(4):581-585, 2011. (HU, CE, PE)

OBJECTIVE: Genuine concerns are being raised as to the potential health risks posed by electromagnetic frequency exposure secondary to mobile phone usage. This study was undertaken to assess and compare potential changes in hearing function at the level of the inner ear and central auditory pathway due to chronic exposure to electromagnetic waves from both global system for mobile communications (GSM) and code division multiple access (CDMA) mobile phone usage. DESIGN: Cohort study. SETTING: Tertiary referral center. SUBJECTS AND METHODS: One hundred twenty-five subjects who were long-term mobile phone users (more than 1 year; 63 GSM and 62 CDMA) and 58 controls who had never used mobile phones underwent audiological investigations including pure tone audiometry (250-12 kHz), tympanometry, distortion product otoacoustic emissions (DPOAE), auditory brain responses (ABR), and middle latency responses (MLRs). The changes in various parameters were studied in mobile-using and non-mobile-using ears of both GSM and CDMA subjects and corresponding ears of the controls to ascertain the effects of electromagnetic exposure. RESULTS: GSM and CDMA users were found to be at a significantly higher risk of having DPOAE absent as compared with controls ($P < .05$). They were found to have higher speech frequency thresholds and lower MLR wave and Na and Pa amplitudes. More than 3 years of mobile phone usage emerged as a risk factor ($P < .05$). The damage done was bilateral, with the quantum of damage being the same for both GSM and CDMA. CONCLUSION: Long-term and intensive GSM and CDMA mobile phone use may cause damage to cochlea as well as the auditory cortex.

(E) Papageorgiou CC, Hountala CD, Maganioti AE, Kyprianou MA, Rabavilas AD, Papadimitriou GN, Capsalis CN. Effects of wi-fi signals on the p300 component of event-related potentials during an auditory hayling task. J Integr Neurosci. 10(2):189-202, 2011 (HU, EE)

The P300 component of event-related potentials (ERPs) is believed to index attention and working memory (WM) operation of the brain. The present study focused on the possible gender-related effects of Wi-Fi (Wireless Fidelity) electromagnetic fields (EMF) on these processes. Fifteen male and fifteen female subjects, matched for age and education level, were investigated while performing a modified version of the Hayling Sentence Completion test adjusted to induce WM. ERPs were recorded at 30 scalp electrodes, both without and with the exposure to a Wi-Fi signal. P300 amplitude values at 18 electrodes were found to be significantly lower in the response inhibition condition than in the response initiation and baseline conditions. Independent of the above effect, within the response inhibition condition there was also a significant gender X radiation interaction effect manifested at 15 leads by decreased P300 amplitudes of males in comparison to female subjects only at the presence of EMF. In conclusion, the present findings suggest that Wi-Fi exposure may exert gender-related alterations on neural activity associated with the amount of attentional resources engaged during a linguistic test adjusted to induce WM.

(NE) Paparini A, Rossi P, Gianfranceschi G, Brugaletta V, Falsaperla R, De Luca P, Romano Spica V. No evidence of major transcriptional changes in the brain of mice exposed to 1800 MHz GSM signal. Bioelectromagnetics. 29(4):312-323, 2008. (AS, CH)

To analyze possible effects of microwaves on gene expression, mice were exposed to global system for mobile communication (GSM) 1800 MHz signal for 1 h at a whole body SAR of 1.1 W/kg. Gene expression was studied in the whole brain, where the average SAR was 0.2 W/kg, by expression microarrays containing over 22,600 probe sets. Comparison of data from sham and exposed animals showed no significant difference in gene expression modulation. However, when less stringent constraints were adopted to analyze microarray results, 75 genes were found to be modulated following exposure. Forty-two probes showed fold changes ranging from 1.5 to 2.8, whereas 33 were down-regulated from 0.67- to 0.29-fold changes, but these differences in gene expression were not confirmed by real-time PCR. Under these specific limited conditions, no consistent indication of gene expression modulation in whole mouse brain was found associated to GSM 1800 MHz exposure.

(E) Parazzini M, Ravazzani P, Tognola G, Thuróczy G, Molnar FB, Sacchettini A, Ardesi G, Mainardi LT. Electromagnetic fields produced by GSM cellular phones and heart rate variability. Bioelectromagnetics. 28(2):122-129, 2007. (HU, PE)

In this study, 26 healthy young volunteers were submitted to 900 MHz (2 W) GSM cellular phone exposure and to sham exposure in separate sessions. The study was designed to assess cardiac regulatory mechanism in different autonomic nervous system (ANS) states during exposure to low-intensity EMF. Rest-to-stand protocol was applied to evaluate ANS in quiet condition (rest, vagal prevalence) and after a sympathetic activation (stand). The procedure is conducted twice in a double-blind design: once with a genuine EMF exposure and once with a sham exposure (at least 24 h apart). During each session three-leads electrocardiograms were recorded and RR series extracted off-line. Time domain and frequency domain HRV parameters were calculated in every phase of the protocol and during different exposures. The analysis of the data show there was no statistically significant effect due to EMF exposure both on main (i.e., RR mean) and most of the other HRV parameters. A weak interaction between some HRV parameters (i.e., SDNN, TINN, and triangular index in time domain and LF power in frequency domain analysis) and RF exposure was observed and this effect seems to be gathered around the sympathetic response to stand.

(NE) Parazzini M, Sibella F, Lutman ME, Mishra S, Moulin A, Sliwinska-Kowalska M, Woznicka E, Politanski P, Zmyslony M, Thuroczy G, Molnár F, Kubinyi G, Tavartkiladze G, Bronyakin S, Uloziene I, Uloza V, Gradauskiene E, Ravazzani P. Effects of UMTS cellular phones on human hearing: results of the European project EMFnEAR. Radiat Res. 172(2):244-251, 2009. (HU, PE)

The European project EMFnEAR was undertaken to assess potential changes in human auditory function after a short-term exposure to radiofrequency (RF) radiation produced by UMTS (Universal Mobile Telecommunication System) mobile phones. Participants were healthy young adults with no hearing or ear disorders. Auditory function was assessed immediately before and after exposure to radiofrequency radiation, and only the exposed ear was tested. Tests for the assessment of auditory function were hearing threshold level (HTL), distortion product otoacoustic emissions (DPOAE), contralateral suppression of transiently evoked otoacoustic emission (CAS effect on TEOAE), and auditory evoked potentials (AEP). The exposure consisted

of speech at a typical conversational level delivered via an earphone to one ear, plus genuine or sham RF-radiation exposure produced by a commercial phone controlled by a personal computer. Results from 134 participants did not show any consistent pattern of effects on the auditory system after a 20-min UMTS exposure at the maximum output of the phone with 69 mW/kg SAR in the cochlea region in a double blind comparison of genuine and sham exposure. An isolated effect on the hearing threshold at high frequencies was identified, but this was statistically nonsignificant after correction for multiple comparisons. It is concluded that UMTS short-term exposure at the maximum output of consumer mobile phones does not cause measurable immediate effects on the human auditory system.

(E) Partsvania B, Sulaberidze T, Shoshiashvili L, Modebadze Z. Acute effect of exposure of mollusk single neuron to 900-MHz mobile phone radiation. Electromagn Biol Med. 30(3):170-179, 2011. (CS, EE)

The goal of the present work was to explore the influence of commercially available cell phone irradiation on the single neuron excitability and memory processes. A Transverse Electromagnetic Cell (TEM Cell) was used to expose single neurons of mollusk to the electromagnetic field. Finite-Difference Time-Domain (FDTD) method was used for modeling the TEM Cell and the electromagnetic field interactions with living nerve ganglion and neurons. Neuron electrophysiology was investigated using standard microelectrode technique. The specific absorption rate (SAR) deposited into the single neuron was calculated to be 0.63 W/kg with a temperature increment of 0.1°C. After acute exposure, average firing threshold of the action potentials was not changed. However, the average latent period was significantly decreased. This indicates that together with latent period the threshold and the time of habituation might be altered during exposure. However, these alterations are transient and only latent period remains on the changed level.

(E) Pelletier A, Delanaud S, Décima P, Thuroczy G, de Seze R, Cerri M, Bach V, Libert JP, Loos N. Effects of chronic exposure to radiofrequency electromagnetic fields on energy balance in developing rats. Environ Sci Pollut Res Int. 20:2735-2746, 2013. (AS, LI, CE, BE, PE, EE, SL)

The effects of radiofrequency electromagnetic fields (RF-EMF) on the control of body energy balance in developing organisms have not been studied, despite the involvement of energy status in vital physiological functions. We examined the effects of chronic RF-EMF exposure (900 MHz, 1 V m(-1)) on the main functions involved in body energy homeostasis (feeding behaviour, sleep and thermoregulatory processes). Thirteen juvenile male Wistar rats were exposed to continuous RF-EMF for 5 weeks at 24 °C of air temperature (T (a)) and compared with 11 non-exposed animals. Hence, at the beginning of the 6th week of exposure, the functions were recorded at T (a) of 24 °C and then at 31 °C. We showed that the frequency of rapid eye movement sleep episodes was greater in the RF-EMF-exposed group, independently of T (a) (+42.1 % at 24 °C and +31.6 % at 31 °C). The other effects of RF-EMF exposure on several sleep parameters were dependent on T (a). At 31 °C, RF-EMF-exposed animals had a

significantly lower subcutaneous tail temperature (-1.21 °C) than controls at all sleep stages; this suggested peripheral vasoconstriction, which was confirmed in an experiment with the vasodilatator prazosin. Exposure to RF-EMF also increased daytime food intake (+0.22 g h(-1)). Most of the observed effects of RF-EMF exposure were dependent on T (a). Exposure to RF-EMF appears to modify the functioning of vasomotor tone by acting peripherally through α-adrenoceptors. The elicited vasoconstriction may restrict body cooling, whereas energy intake increases. Our results show that RF-EMF exposure can induce energy-saving processes without strongly disturbing the overall sleep pattern.

(E) Pelletier A, Delanaud S, de Seze R, Bach V, Libert JP, Loos N. Does Exposure to a Radiofrequency Electromagnetic Field Modify Thermal Preference in Juvenile Rats? PLoS One. 2014 Jun 6;9(6):e99007. (AS, LI, CE, BE, PE, EE, SL)

Some studies have shown that people living near a mobile phone base station may report sleep disturbances and discomfort. Using a rat model, we have previously shown that chronic exposure to a low-intensity radiofrequency electromagnetic field (RF-EMF) was associated with paradoxical sleep (PS) fragmentation and greater vasomotor tone in the tail. Here, we sought to establish whether sleep disturbances might result from the disturbance of thermoregulatory processes by a RF-EMF. We recorded thermal preference and sleep stage distribution in 18 young male Wistar rats. Nine animals were exposed to a low-intensity RF-EMF (900 MHz, 1 V.m-1) for five weeks and nine served as non-exposed controls. Thermal preference was assessed in an experimental chamber comprising three interconnected compartments, in which the air temperatures (Ta) were set to 24°C, 28°C and 31°C. Sleep and tail skin temperature were also recorded. Our results indicated that relative to control group, exposure to RF-EMF at 31°C was associated with a significantly lower tail skin temperature (-1.6°C) which confirmed previous data. During the light period, the exposed group preferred to sleep at Ta = 31°C and the controls preferred Ta = 28°C. The mean sleep duration in exposed group was significantly greater (by 15.5%) than in control group (due in turn to a significantly greater amount of slow wave sleep (SWS, +14.6%). Similarly, frequency of SWS was greater in exposed group (by 4.9 episodes.h-1). The PS did not differ significantly between the two groups. During the dark period, there were no significant intergroup differences. We conclude that RF-EMF exposure induced a shift in thermal preference towards higher temperatures. The shift in preferred temperature might result from a cold thermal sensation. The change in sleep stage distribution may involve signals from thermoreceptors in the skin. Modulation of SWS may be a protective adaptation in response to RF-EMF exposure.

(NE) Perentos N, Croft RJ, McKenzie RJ, Cvetkovic D, Cosic I. Comparison of the effects of continuous and pulsed mobile phone like RF exposure on the human EEG. Australas Phys Eng Sci Med. 30(4):274-280, 2007. (HU, EE)

It is not clear yet whether Global System for Mobiles (GSM) mobile phone radiation has the ability to interfere with normal resting brain function. There have been reports that GSM exposure increases alpha band power, and does so only when the signal is modulated at low

frequencies (Huber, R., Treyer, V., Borbely, A. A., Schuderer, J., Gottselig, J. M., Landolt, H.P., Werth, E., Berthold,T., Kuster, N., Buck, A and Achermann, P. Electromagnetic fields, such as those from mobile phones, alter regional cerebral blood flow and sleep and waking EEG. J Sleep Res 11, 289-295, 2002.) However, as that research employed exposure distributions that are not typical of normal GSM handset usage (deep brain areas were overexposed), it remains to be determined whether a similar result patterning would arise from a more representative exposure. In this fully counterbalanced cross-over design, we recruited 12 participants and tried to replicate the modulation linked post exposure alpha band power increase described above, but with an exposure source (dipole antenna) more closely resembling that of a real GSM handset. Exposures lasted for 15 minutes. No changes to alpha power were found for either modulated or unmodulated radiofrequency fields, and thus we failed to replicate the above results. Possible reasons for this failure to replicate are discussed, with the main reason argued to be the lower and more representative exposure distribution employed in the present study. In addition we investigated the possible GSM exposure related effects on the non-linear features of the resting electroencephalogram using the Approximate Entropy (ApEn) method of analysis. Again, no effect was demonstrated for either modulated or unmodulated radiofrequency exposures.

(E) Perentos N, Croft RJ, McKenzie RJ, Cosic I. The alpha band of the resting electroencephalogram under pulsed and continuous radio frequency exposures. IEEE Trans Biomed Eng. 60(6):1702-1710, 2013. (HU, EE)

The effect of GSM-like electromagnetic fields with the resting electroencephalogram (EEG) alpha band activity was investigated in a double-blind cross-over experimental paradigm, testing the hypothesis that pulsed but not continuous radio frequency (RF) exposure would affect alpha activity, and the hypothesis that GSM-like pulsed low frequency fields would affect alpha. Seventy-two healthy volunteers attended a single recording session where the eyes open resting EEG activity was recorded. Four exposure intervals were presented (sham, pulsed modulated RF, continuous RF, and pulsed low frequency) in a counterbalanced order where each exposure lasted for 20 min. Compared to sham, a suppression of the global alpha band activity was observed under the pulsed modulated RF exposure, and this did not differ from the continuous RF exposure. No effect was seen in the extremely low frequency condition. That there was an effect of pulsed RF that did not differ significantly from continuous RF exposure does not support the hypothesis that "pulsed" RF is required to produce EEG effects. The results support the view that alpha is altered by RF electromagnetic fields, but suggest that the pulsing nature of the fields is not essential for this effect to occur.

(NE) Platano D, Mesirca P, Paffi A, Pellegrino M, Liberti M, Apollonio F, Bersani F, Aicardi G. Acute exposure to low-level CW and GSM-modulated 900 MHz radiofrequency does not affect Ba 2+ currents through voltage-gated calcium channels in rat cortical neurons. Bioelectromagnetics. 28(8):599-607, 2007. (CS, EE)

We have studied the non-thermal effects of radiofrequency (RF) electromagnetic fields (EMFs) on Ba(2+) currents (I Ba 2+) through voltage-gated calcium channels (VGCC), recorded in primary cultures of rat cortical neurons using the patch-clamp technique. To assess whether low-level acute RF field exposure could modify the amplitude and/or the voltage-dependence of I Ba 2+, Petri dishes containing cultured neurons were exposed for 1-3 periods of 90 s to 900 MHz RF-EMF continuous wave (CW) or amplitude-modulated according to global system mobile

communication standard (GSM) during whole-cell recording. The specific absorption rates (SARs) were 2 W/kg for CW and 2 W/kg (time average value) for GSM-modulated signals, respectively. The results obtained indicate that single or multiple acute exposures to either CW or GSM-modulated 900 MHz RF-EMFs do not significantly alter the current amplitude or the current-voltage relationship of I Ba 2+, through VGCC.

(NE) Poulletier de Gannes F, Haro E, Hurtier A, Taxile M, Ruffié G, Billaudel B, Veyret B, Lagroye I. Effect of exposure to the edge signal on oxidative stress in brain cell models. Radiat Res. 175(2):225-230, 2011. (CS, OX)

In this study we investigated the effect of the Enhanced Data rate for GSM Evolution (EDGE) signal on cells of three human brain cell lines, SH-SY5Y, U87 and CHME5, used as models of neurons, astrocytes and microglia, respectively, as well as on primary cortical neuron cultures. SXC-1800 waveguides (IT'IS-Foundation, Zürich, Switzerland) were modified for in vitro exposure to the EDGE signal radiofrequency (RF) radiation at 1800 MHz. Four exposure conditions were tested: 2 and 10 W/kg for 1 and 24 h. The production of reactive oxygen species (ROS) was measured by flow cytometry using the dichlorofluorescein diacetate (DCFH-DA) probe at the end of the 24-h exposure or 24 h after the 1-h exposure. Rotenone treatment was used as a positive control. All cells tested responded to rotenone treatment by increasing ROS production. These findings indicate that exposure to the EDGE signal does not induce oxidative stress under these test conditions, including 10 W/kg. Our results are in agreement with earlier findings that RF radiation alone does not increase ROS production.

(NE) Poulletier de Gannes F, Masuda H, Billaudel B, Poque-Haro E, Hurtier A, Lévêque P, Ruffié G, Taxile M, Veyret B, Lagroye I. Effects of GSM and UMTS mobile telephony signals on neuron degeneration and blood-brain barrier permeation in the rat brain. Sci Rep. 7(1):15496, 2017. (AS, CE, ME)

Blood-brain barrier (BBB) permeation and neuron degeneration were assessed in the rat brain following exposure to mobile communication radiofrequency (RF) signals (GSM-1800 and UMTS-1950). Two protocols were used: (i) single 2 h exposure, with rats sacrificed immediately, and 1 h, 1, 7, or 50 days later, and (ii) repeated exposures (2 h/day, 5 days/week, for 4 weeks) with the effects assessed immediately and 50 days after the end of exposure. The rats' heads were exposed at brain-averaged specific absorption rates (BASAR) of 0.026, 0.26, 2.6, and 13 W/kg. No adverse impact in terms of BBB leakage or neuron degeneration was observed after single exposures or immediately after the end of repeated exposure, with the exception of a transient BBB leakage (UMTS, 0.26 W/kg). Fifty days after repeated exposure, the occurrence of degenerating neurons was unchanged on average. However, a significant increased albumin leakage was detected with both RF signals at 13 W/kg. In this work, the strongest, delayed effect was induced by GSM-1800 at 13 W/kg. Considering that 13 W/kg BASAR in the rat head is equivalent to 4 times as much in the human head, deleterious effects may occur following repeated human brain exposure above 50 W/kg.

(NE) Prochnow N, Gebing T, Ladage K, Krause-Finkeldey D, El Ouardi A, Bitz A, Streckert J, Hansen V, Dermietzel R. Electromagnetic field effect or simply stress? Effects of UMTS exposure on hippocampal longterm plasticity in the context of procedure related hormone release. PLoS One. 6(5):e19437, 2011. (AS, EE)

Harmful effects of electromagnetic fields (EMF) on cognitive and behavioural features of humans and rodents have been controversially discussed and raised persistent concern about adverse effects of EMF on general brain functions. In the present study we applied radio-frequency (RF) signals of the Universal Mobile Telecommunications System (UMTS) to full brain exposed male Wistar rats in order to elaborate putative influences on stress hormone release (corticosteron; CORT and adrenocorticotropic hormone; ACTH) and on hippocampal derived synaptic long-term plasticity (LTP) and depression (LTD) as electrophysiological hallmarks for memory storage and memory consolidation. Exposure was computer controlled providing blind conditions. Nominal brain-averaged specific absorption rates (SAR) as a measure of applied mass-related dissipated RF power were 0, 2, and 10 W/kg over a period of 120 min. Comparison of cage exposed animals revealed, regardless of EMF exposure, significantly increased CORT and ACTH levels which corresponded with generally decreased field potential slopes and amplitudes in hippocampal LTP and LTD. Animals following SAR exposure of 2 W/kg (averaged over the whole brain of 2.3 g tissue mass) did not differ from the sham-exposed group in LTP and LTD experiments. In contrast, a significant reduction in LTP and LTD was observed at the high power rate of SAR (10 W/kg). The results demonstrate that a rate of 2 W/kg displays no adverse impact on LTP and LTD, while 10 W/kg leads to significant effects on the electrophysiological parameters, which can be clearly distinguished from the stress derived background. Our findings suggest that UMTS exposure with SAR in the range of 2 W/kg is not harmful to critical markers for memory storage and memory consolidation, however, an influence of UMTS at high energy absorption rates (10 W/kg) cannot be excluded.

(E) Qiao S, Peng R, Yan H, Gao Y, Wang C, Wang S, Zou Y, Xu X, Zhao L, Dong J, Su Z, Feng X, Wang L, Hu X. Reduction of Phosphorylated Synapsin I (Ser-553) Leads to Spatial Memory Impairment by Attenuating GABA Release after Microwave Exposure in Wistar Rats. PLoS One. 9(4):e95503, 2014. (AS, CS, BE, CH)

BACKGROUND: Abnormal release of neurotransmitters after microwave exposure can cause learning and memory deficits. This study investigated the mechanism of this effect by exploring the potential role of phosphorylated synapsin I (p-Syn I). METHODS: Wistar rats, rat hippocampal synaptosomes, and differentiated (neuronal) PC12 cells were exposed to microwave radiation for 5 min at a mean power density of 30 mW/cm2. Sham group rats, synaptosomes, and cells were otherwise identically treated and acted as controls for all of the following post-exposure analyses. Spatial learning and memory in rats was assessed using the Morris Water Maze (MWM) navigation task. The protein expression and presynaptic distribution of p-Syn I and neurotransmitter transporters were examined via western blotting and immunoelectron microscopy, respectively. Levels amino acid neurotransmitter release from rat hippocampal synaptosomes and PC12 cells were measured using high performance liquid chromatograph (HPLC) at 6 hours after exposure, with or without synapsin I silencing via

shRNA transfection. RESULTS: In the rat experiments, there was a decrease in spatial memory performance after microwave exposure. The expression of p-Syn I (ser-553) was decreased at 3 days post-exposure and elevated at later time points. Vesicular GABA transporter (VGAT) was significantly elevated after exposure. The GABA release from synaptosomes was attenuated and p-Syn I (ser-553) and VGAT were both enriched in small clear synaptic vesicles, which abnormally assembled in the presynaptic terminal after exposure. In the PC12 cell experiments, the expression of p-Syn I (ser-553) and GABA release were both attenuated at 6 hours after exposure. Both microwave exposure and p-Syn I silencing reduced GABA release and maximal reduction was found for the combination of the two, indicating a synergetic effect. CONCLUSION: p-Syn I (ser-553) was found to play a key role in the impaired GABA release and cognitive dysfunction that was induced by microwave exposure.

(E) Qin F, Yuan H, Nie J, Cao Y, Tong J. [Effects of nano-selenium on cognition performance of mice exposed in 1800 MHz radiofrequency fields]. Wei Sheng Yan Jiu. 43(1):16-21, 2014. [Article in Chinese] (AS, CE, BE, CH, OX)

OBJECTIVE: To study the effects of nano-selenium (NSe) on cognition performance of mice exposed to 1800 MHz radiofrequency fields (RF).METHODS: Male mice were randomly divided into four groups, control and nano-Se low, middle and high dose groups (L, M, H). Each group was sub-divided into three groups, RF 0 min, RF 30 min and RF 120 min. Nano-se solution (2, 4 and 8 microg/ml) were administered to mice of L, M, H groups by intra-gastric injection respectively, 0.5 ml/d for 50 days, the control group was administered with distilled water. At the 21st day, the mice in RF subgroup were exposed to 208 microW/cm2 1800 MHz radiofrequency fields (0, 30 and 120 min/d respectively) for 30 days. The cognitive ability of the mice were tested with Y-maze. Further, the levels of MDA, GABA, Glu, Ach and the activities of CAT and GSH-Px in cerebra were measured. RESULTS: Significant impairments in learning and memory ($P < 0.05$) were observed in the RF 120 min group, and with reduction of the Ach level and the activities of CAT and GSH-Px and increase of the content of GABA, Glu and MDA in cerebrum. NSe enhanced cognitive performance of RF mice, decreased GABA, Glu and MDA levels, increased Ach levels, GSH-Px and CAT activities. CONCLUSION: NSe could improve cognitive impairments of mice exposed to RF, the mechanism of which might involve the increasing antioxidation, decreasing free radical content and the changes of cerebra neurotransmitters.

(NE) Rağbetli MC, Aydinlioğlu A, Koyun N, Rağbetli C, Karayel M. Effect of prenatal exposure to mobile phone on pyramidal cell numbers in the mouse hippocampus: a stereological study. Int J Neurosci. 119(7):1031-1041, 2009. (AS, ME, DE)

Because of the possible risk factor for the health, World Health Organization (WHO) recommended the study with animals on the developing nervous system concerning the exposure to radiofrequency (RF) field. A few studies related to hippocampal exposure are available, which indicate the impact of RF field in some parameters. The present study investigated the effect of exposure to mobile phone on developing hippocampus. Male and

female Swiss albino mice were housed as control and mobile phone exposed groups. The pregnant animals in tested group were exposed to the effects of mobile phone in a room possessing the exposure system. The left hemispheres of the brains were processed by frozen microtome. The sections obtained were stained with Hematoxylin & Eosin. For cell counting by the optical fractionator method, a pilot study was first performed. Hippocampal areas were analyzed using Axiovision software running on a personal computer. The optical dissector, systematically and randomly spaced, was focused to the widest profile of the pyramidal cell nucleus. No significant difference in pyramidal cell number of total Cornu Ammonis (CA) sectors of hippocampus was found between the control and the mobile phone exposed groups ($p > .05$). It was concluded that further study is needed in this field due to popular use of mobile telephones and relatively high exposure to the developing brain.

(E) Rağbetli MC, Aydinlioğlu A, Koyun N, Rağbetli C, Bektas S, Ozdemir S. The effect of mobile phone on the number of Purkinje cells: a stereological study. Int J Radiat Biol. 86(7):548-554, 2010. (AS, ME, DE)

PURPOSE: The World Health Organisation proposed an investigation concerning the exposure of animals to radiofrequency fields because of the possible risk factor for health. At power frequencies there is evidence to associate both childhood leukaemia and brain tumours with magnetic field exposures. There is also evidence of the effect of mobile phone exposure on both cognitive functions and the cerebellum. Purkinje cells of the cerebellum are also sensitive to high dose microwave exposure in rats. The present study investigated the effect of exposure to mobile phone on the number of Purkinje and granule neurons in the developing cerebellum. **MATERIAL AND METHODS:** Male and female Swiss albino mice were housed as control and mobile phone-exposed groups. Pregnant animals in the experimental group were exposed to Global System for Mobile Communication (GSM) mobile phone radiation at 890-915 MHz at 0.95 W/Kg specific absorption rate (SAR). The cerebella were processed by frozen microtome. The sections obtained were stained with Haematoxylin-eosin and cresyl violet. For cell counting by the optical fractionator method, a pilot study was firstly performed. Cerebellar areas were analysed by using Axiovision software running on a personal computer. The optical dissectors were systematically spaced at random, and focused to the widest profile of the neuron cell nucleus. **RESULTS:** A significant decrease in the number of Purkinje cells and a tendency for granule cells to increase in cerebellum was found. **CONCLUSION:** Further studies in this area are needed due to the popular use of mobile telephones and relatively high exposure on developing brain.

(E) Razavinasab M, Moazzami K, Shabani M. Maternal mobile phone exposure alters intrinsic electrophysiological properties of CA1 pyramidal neurons in rat offspring. Toxicol Ind Health. 32:968-979, 2016. (AS, CE, BE, DE, EE)

Some studies have shown that exposure to electromagnetic field (EMF) may result in structural damage to neurons. In this study, we have elucidated the alteration in the hippocampal function of offspring Wistar rats (n = 8 rats in each group) that were chronically exposed to mobile phones during their gestational period by applying behavioral, histological, and

electrophysiological tests. Rats in the EMF group were exposed to 900 MHz pulsed-EMF irradiation for 6 h/day. Whole cell recordings in hippocampal pyramidal cells in the mobile phone groups did show a decrease in neuronal excitability. Mobile phone exposure was mostly associated with a decrease in the number of action potentials fired in spontaneous activity and in response to current injection in both male and female groups. There was an increase in the amplitude of the afterhyperpolarization (AHP) in mobile phone rats compared with the control. The results of the passive avoidance and Morris water maze assessment of learning and memory performance showed that phone exposure significantly altered learning acquisition and memory retention in male and female rats compared with the control rats. Light microscopy study of brain sections of the control and mobile phone-exposed rats showed normal morphology. Our results suggest that exposure to mobile phones adversely affects the cognitive performance of both female and male offspring rats using behavioral and electrophysiological techniques.

(E) Redmayne M, Smith E, and Abramson MJ. The relationship between adolescents' well-being and their wireless phone use: a cross-sectional study. Environmental Health 12(1):90, 2013. (HU, BE)

Background. The exposure of young people to radiofrequency electromagnetic fields (RF-EMFs) has increased rapidly in recent years with their increased use of cellphones and use of cordless phones and WiFi. We sought to ascertain associations between New Zealand early-adolescents' subjective well-being and self-reported use of, or exposure to, wireless telephone and internet technology. Methods. In this cross-sectional survey, participants completed questionnaires in class about their cellphone and cordless phone use, their self-reported well-being, and possible confounding information such as whether they had had influenza recently or had a television in the bedroom. Parental questionnaires provided data on whether they had WiFi at home and cordless phone ownership and model. Data were analysed with Ordinal Logistic Regression adjusting for common confounders. Odds ratios (OR) and 95% confidence intervals were calculated. Results. The number and duration of cellphone and cordless phone calls were associated with increased risk of headaches (>6 cellphone calls over 10 minutes weekly, adjusted OR 2.4, CI 1.2-4.8; >15 minutes cordless use daily adjusted OR 1.74, CI 1.1-2.9)). Texting and extended use of wireless phones was related to having a painful 'texting' thumb). Using a wired cellphone headset was associated with tinnitus (adjusted OR 1.8, CI 1.0-3.3), while wireless headsets were associated with headache (adjusted OR 2.2, CI 1.1-4.5), feeling down/depressed (adjusted OR 2.0, CI 1.1-3.8), and waking in the night (adjusted OR 2.4, CI 1.2-4.8). Several cordless phone frequencies bands were related to tinnitus, feeling down/depressed and sleepiness at school, while the last of these was also related to modulation. Waking nightly was less likely for those with WiFi at home (adjusted OR 0.7, CI 0.4-0.99). Being woken at night by a cellphone was strongly related to tiredness at school (OR 4.1, CI 2.2-7.7). Conclusions . There were more statistically significant associations (36%) than could

be expected by chance (5%). Several were dose-dependent relationships. To safeguard young people's well-being, we suggest limiting their use of cellphones and cordless phones to less than 15 minutes daily, and employing a speaker-phone device for longer daily use. We recommend parental measures are taken to prevent young people being woken by their cellphones.

(NE) Redmayne M, Smith CL, Benke G, Croft RJ, Dalecki A, Dimitriadis C, Kaufman J, Macleod S, Sim MR, Wolfe R, Abramson MJ. Use of mobile and cordless phones and cognition in Australian primary school children: a prospective cohort study. Environ Health. 15(1):26, 2016. (HU, CE, BE)

BACKGROUND: Use of mobile (MP) and cordless phones (CP) is common among young children, but whether the resulting radiofrequency exposure affects development of cognitive skills is not known. Small changes have been found in older children. This study focused on children's exposures to MP and CP and cognitive development. The hypothesis was that children who used these phones would display differences in cognitive function compared to those who did not. METHODS: We recruited 619 fourth-grade students (8-11 years) from 37 schools around Melbourne and Wollongong, Australia. Participants completed a short questionnaire, a computerised cognitive test battery, and the Stroop colour-word test. Parents completed exposure questionnaires on their child's behalf. Analysis used multiple linear regression. The principal exposure-metrics were the total number of reported MP and CP calls weekly categorised into no use ('None'); use less than or equal to the median amount ('Some'); and use more than the median ('More'). The median number of calls/week was 2.5 for MP and 2.0 for CP. RESULTS: MP and CP use for calls was low; and only 5 of 78 comparisons of phone use with cognitive measures were statistically significant. The reaction time to the response-inhibition task was slower in those who used an MP 'More' compared to the 'Some' use group and non-users. For CP use, the response time to the Stroop interference task was slower in the 'More' group versus the 'Some' group, and accuracy was worse in visual recognition and episodic memory tasks and the identification task. In an additional exploratory analysis, there was some evidence of a gender effect on mean reaction times. The highest users for both phone types were girls. CONCLUSIONS: Overall, there was little evidence cognitive function was associated with CP and MP use in this age group. Although there was some evidence that effects of MP and CP use on cognition may differ by gender, this needs further exploration. CP results may be more reliable as parents estimated children's phone use and the CPs were at home; results for CP use were broadly consistent with our earlier study of older children.

(E) Regel SJ, Tinguely G, Schuderer J, Adam M, Kuster N, Landolt HP, Achermann P. Pulsed radio-frequency electromagnetic fields: dose-dependent effects on sleep, the sleep EEG and cognitive performance. J Sleep Res. 16(3):253-258, 2007. (HU, EE, BE, SL)

To establish a dose-response relationship between the strength of electromagnetic fields (EMF) and previously reported effects on the brain, we investigated the influence of EMF exposure by varying the signal intensity in three experimental sessions. The head of 15 healthy male subjects was unilaterally exposed for 30 min prior to sleep to a pulse-modulated EMF (GSM handset like signal) with a 10 g-averaged peak spatial specific absorption rate of (1) 0.2 W kg(-1), (2) 5 W kg(-1), or (3) sham exposed in a double-blind, crossover design. During exposure, subjects performed two series of three computerized cognitive tasks, each presented in a fixed order [simple reaction time task, two-choice reaction time task (CRT), 1-, 2-, 3-back task]. Immediately after exposure, night-time sleep was polysomnographically recorded for 8 h. Sleep architecture was not affected by EMF exposure. Analysis of the sleep electroencephalogram (EEG) revealed a dose-dependent increase of power in the spindle frequency range in non-REM sleep. Reaction speed decelerated with increasing field intensity in the 1-back task, while accuracy in the CRT and N-back task were not affected in a dose-dependent manner. In summary, this study reveals first indications of a dose-response relationship between EMF field intensity and its effects on brain physiology as demonstrated by changes in the sleep EEG and in cognitive performance.

(NE) Riddervold IS, Pedersen GF, Andersen NT, Pedersen AD, Andersen JB, Zachariae R, Mølhave L, Sigsgaard T, Kjaergaard SK. Cognitive function and symptoms in adults and adolescents in relation to rf radiation from UMTS base stations. Bioelectromagnetics. 29(4):257-267, 2008. (HU, BE)

There is widespread public concern about the potential adverse health effects of mobile phones in general and their associated base stations in particular. This study was designed to investigate the acute effects of radio frequency (RF) electromagnetic fields (EMF) emitted by the Universal Mobile Telecommunication System (UMTS) mobile phone base stations on human cognitive function and symptoms. Forty adolescents (15-16 years) and 40 adults (25-40 years) were exposed to four conditions: (1) sham, (2) a Continuous Wave (CW) at 2140 MHz, (3) a signal at 2140 MHz modulated as UMTS and (4) UMTS at 2140 MHz including all control features in a randomized, double blinded cross-over design. Each exposure lasted 45 min. During exposure the participants performed different cognitive tasks with the Trail Making B (TMB) test as the main outcome and completed a questionnaire measuring self reported subjective symptoms. No statistically significant differences between the UMTS and sham conditions were found for performance on TMB. For the adults, the estimated difference between UMTS and sham was -3.2% (-9.2%; 2.9%) and for the adolescents 5.5% (-1.1%; 12.2%). No significant changes were found in any of the cognitive tasks. An increase in 'headache rating' was observed when data from the adolescents and adults were combined (P = 0.027), an effect that may be due to differences at baseline. In conclusion, the primary hypothesis that UMTS radiation reduces general performance in the TMB test was not confirmed. However, we suggest that the hypothesis of subjective symptoms and EMF exposure needs further research.

(E) Roggeveen S, van Os J, Viechtbauer W, Lousberg R. EEG Changes Due to Experimentally Induced 3G Mobile Phone Radiation. PLoS One. 10(6):e0129496, 2015. (HU, EE)

The aim of this study was to investigate whether a 15-minute placement of a 3G dialing mobile phone causes direct changes in EEG activity compared to the placement of a sham phone. Furthermore, it was investigated whether placement of the mobile phone on the ear or the heart would result in different outcomes. Thirty-one healthy females participated. All subjects were measured twice: on one of the two days the mobile phone was attached to the ear, the other day to the chest. In this single-blind, cross-over design, assessments in the sham phone condition were conducted directly preceding and following the mobile phone exposure. During each assessment, EEG activity and radiofrequency radiation were recorded jointly. Delta, theta, alpha, slow beta, fast beta, and gamma activity was computed. The association between radiation exposure and the EEG was tested using multilevel random regression analyses with radiation as predictor of main interest. Significant radiation effects were found for the alpha, slow beta, fast beta, and gamma bands. When analyzed separately, ear location of the phone was associated with significant results, while chest placement was not. The results support the notion that EEG alterations are associated with mobile phone usage and that the effect is dependent on site of placement. Further studies are required to demonstrate the physiological relevance of these findings.

(E) Roggeveen S, van Os J, Lousberg R. Does the Brain Detect 3G Mobile Phone Radiation Peaks? An Explorative In-Depth Analysis of an Experimental Study. PLoS One. 10(5):e0125390, 2015. (HU, EE)

This study aimed to investigate whether third generation mobile phone radiation peaks result in event related potentials. Thirty-one healthy females participated. In this single-blind, cross-over design, a 15 minute mobile phone exposure was compared to two 15 minute sham phone conditions, one preceding and one following the exposure condition. Each participant was measured on two separate days, where mobile phone placement was varied between the ear and heart. EEG activity and radiofrequency radiation were recorded jointly. Epochs of 1200ms, starting 200ms before and lasting until 1000ms after the onset of a radiation peak, were extracted from the exposure condition. Control epochs were randomly selected from the two sham phone conditions. The main a-priori hypothesis to be tested concerned an increase of the area in the 240-500ms post-stimulus interval, in the exposure session with ear-placement. Using multilevel regression analyses the placement*exposure interaction effect was significant for the frontal and central cortical regions, indicating that only in the mobile phone exposure with ear-placement an enlarged cortical reactivity was found. Post-hoc analyses based on visual inspection of the ERPs showed a second significantly increased area between 500-1000ms post-stimulus for almost every EEG location measured. It was concluded that, when a dialing mobile phone is placed on the ear, its radiation, although unconsciously, is electrically detected by the brain. The question of whether or not this cortical reactivity results in a negative health outcome has to be answered in future longitudinal experiments.

(NE) Roser K, Schoeni A, Röösli M. Mobile phone use, behavioural problems and concentration capacity in adolescents: A prospective study. Int J Hyg Environ Health.; 219(8):759-769, 2016. (HU, BE)

The aim of this study is to prospectively investigate whether exposure to radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phones and other wireless communication devices is related to behavioural problems or concentration capacity in adolescents. The HERMES (Health Effects Related to Mobile phonE use in adolescentS) study sample consisted of 439 Swiss adolescents aged 12-17 years. Behavioural problems were assessed using the Strengths and Difficulties Questionnaire (SDQ), concentration capacity of the adolescents was measured by means of a standardized computerized cognitive test named FAKT. Cross-sectional and longitudinal (1year of follow-up) analyses were performed to investigate possible associations between behavioural problems and concentration capacity and different exposure measures: self-reported and operator-recorded wireless communication device use, cumulative RF-EMF brain and whole body dose and measured personal RF-EMF exposure. In the cross-sectional analyses behavioural problems were associated with several self-reported wireless device use measures but not operator-recorded mobile phone use measures, concentration capacity was associated with several self-reported and operator-recorded exposures. The longitudinal analyses point towards absence of associations. The lack of consistent exposure-response patterns in the longitudinal analyses suggests that behavioural problems and concentration capacity are not affected by the use of wireless communication devices or RF-EMF exposure. Information bias and reverse causality are likely explanations for the observed cross-sectional findings.

(E) Şahin A, Aslan A, Baş O, İkinci A, Özyılmaz C, Fikret Sönmez O, Çolakoğlu S, Odacı E. Deleterious impacts of a 900MHz electromagnetic field on hippocampal pyramidal neurons of 8-week-old Sprague Dawley male rats. Brain Res. 1624:232-238, 2015. (AS, CE, ME)

Children are at potential risk due to their intense use of mobile phones. We examined 8-week-old rats because that age is comparable with the preadolescent period in humans. The numbers of pyramidal neurons in the cornu ammonis of the Sprague Dawley male rat (8-weeks old, weighing 180-250g) hippocampus following exposure to a 900MHz (MHz) electromagnetic field (EMF) were examined. The study consisted of control (CN-G), sham exposed (SHM-EG) and EMF exposed (EMF-EG) groups, 6 rats in each. The EMF-EG rats were exposed to 900MHz EMF (1h/day for 30 days) in an EMF jar. The SHM-EG rats were placed in the EMF jar but not exposed to EMF (1h/day for 30 days). The CN-G rats were not placed into the exposure jar and were not exposed to EMF during the study period. All animals were sacrificed at the end of the experiment, and their brains were removed for histopathological and stereological analysis. The number of pyramidal neurons in the cornu ammonis of the hippocampus was estimated on Cresyl violet stained sections of the brain using the optical dissector counting technique. Histopathological evaluations were also performed on these sections. Histopathological observation showed abundant cells with abnormal, black or dark blue cytoplasm and shrunken morphology among the normal pyramidal neurons. The largest lateral ventricles were observed in the EMF-EG sections compared to those from the other groups. Stereological analyses showed that the total number of pyramidal neurons in the cornu ammonis of the EMF-EG rats was significantly lower than those in CN-G ($p<0.05$) and SHM-EG ($p<0.05$). In conclusion, our results suggest that pyramidal neuron loss and histopathological changes in the cornu ammonis of 8-week-old male rats may be due to 900MHz EMF exposure.

(E) Saikhedkar N, Bhatnagar M, Jain A, Sukhwal P, Sharma C, Jaiswal N. Effects of mobile phone radiation (900 MHz radiofrequency) on structure and functions of rat brain. Neurol Res. 36:1072-1076, 2014. (AS, CE, BE, CC, OX)

Objectives: The goals of this study were: (1) to obtain basic information about the effects of long-term use of mobile phone on cytological makeup of the hippocampus in rat brain (2) to evaluate the effects on antioxidant status, and (3) to evaluate the effects on cognitive behavior particularly on learning and memory. Methods: Rats (age 30 days, 120 ± 5 g) were exposed to 900 MHz radio waves by means of a mobile hand set for 4 hours per day for 15 days. Effects on anxiety, spatial learning, and memory were studied using open field test, elevated plus maze, Morris water maze (MWM), and classic maze test. Effects on brain antioxidant status were also studied. Cresyl violet staining was done to access the neuronal damage. Result: A significant change in behavior, i.e., more anxiety and poor learning was shown by test animals as compared to controls and sham group. A significant change in level of antioxidant enzymes and non-enzymatic antioxidants, and increase in lipid peroxidation were observed in test rats. Histological examination showed neurodegenerative cells in hippocampal sub regions and cerebral cortex. Discussion: Thus our findings indicate extensive neurodegeneration on exposure to radio waves. Increased production of reactive oxygen species due to exhaustion of enzymatic and non-enzymatic antioxidants and increased lipid peroxidation are indicating extensive neurodegeneration in selective areas of CA1, CA3, DG, and cerebral cortex. This extensive neuronal damage results in alterations in behavior related to memory and learning.

(NE) Sakurai T, Kiyokawa T, Narita E, Suzuki Y, Taki M, Miyakoshi J. Analysis of gene expression in a human-derived glial cell line exposed to 2.45 GHz continuous radiofrequency electromagnetic fields. J Radiat Res. 52(2):185-192, 2011. (CS, CH)

The increasing use of mobile phones has aroused public concern regarding the potential health risks of radiofrequency (RF) fields. We investigated the effects of exposure to RF fields (2.45 GHz, continuous wave) at specific absorption rate (SAR) of 1, 5, and 10 W/kg for 1, 4, and 24 h on gene expression in a normal human glial cell line, SVGp12, using DNA microarray. Microarray analysis revealed 23 assigned gene spots and 5 non-assigned gene spots as prospective altered gene spots. Twenty-two genes out of the 23 assigned gene spots were further analyzed by reverse transcription-polymerase chain reaction to validate the results of microarray, and no significant alterations in gene expression were observed. Under the experimental conditions used in this study, we found no evidence that exposure to RF fields affected gene expression in SVGp12 cells.

(NE) **Salunke BP, Umathe SN, Chavan JG. Behavioral in-effectiveness of high frequency electromagnetic field in mice. Physiol Behav. 140:32-37, 2015. (AS, CE, BE)**

The present investigation was carried out with an objective to study the influence of high frequency electromagnetic field (HF-EMF) on anxiety, obsessive compulsive disorder (OCD) and depression-like behavior. For exposure to HF-EMF, non-magnetic material was used to fabricate the housing. Mice were exposed to HF-EMF (2.45 GHz), 60 min/day for 7 or 30 or 60 or 90 or

120 days. The exposure was carried out by switching-on inbuilt class-I BLUETOOTH device that operates on 2.45 GHz frequency in file transfer mode at a peak density of 100mW. Mice were subjected to the assessment of anxiety, OCD and depression-like behavior for 7 or 30 or 60 or 90 or 120days of exposure. The anxiety-like behavior was assessed by elevated plus maze, open field test and social interaction test. OCD-like behavior was assessed by marble burying behavior, whereas depression-like behavior was assessed by forced swim test and tail suspension test. The present experiment demonstrates that up to 120days of exposure to HF-EMF does not produce anxiety, OCD and depression-like behavior in mice.

(E) Sarapultseva EI, Igolkina JV, Tikhonov VN, Dubrova YE.THE IN VIVO EFFECTS OF LOW-INTENSITY RADIOFREQUENCY FIELDS ON THE MOTOR ACTIVITY OF PROTOZOA. Int J Radiat Biol. 90:262-267, 2014. (AS, BE, LI)

Purpose: To analyze the direct and transgenerational effects of exposure to low-dose 1 GHz (mobile phone/wireless telecommunication range) and 10 GHz (radar/satellite communication range) radiofrequency electromagnetic fields (RF-EMF) on the motility of ciliates Spirostomum ambiguum. Materials and Methods: S. ambiguum were exposed to 1 GHz and 10 GHz RF-EMF with power flux densities (PD) ranging from 0.05 to 0.5 W/m^2 over a period of time from 0.05 to 10 h. The motility of directly exposed ciliates and their non-exposed progeny across 10-15 generations was measured. Results: Exposure to 0.1 W/m^2 of either 1 or 10 GHz RF-EMF resulted in a significant decrease in the motility. The dose of exposure capable of altering the mobility of ciliates was inversely correlated with the flux density of RF-EMF. The motility of the non-exposed progeny of ciliates irradiated with 0.1 W/m^2 of 10 GHz RF-EMF remained significantly compromised, at least, across 10-15 generations, thus indicating the presence of transgenerational effects. Conclusions: The results of our study show that low-dose exposure to RF-EMF can significantly affect the motility of irradiated ciliates and their non-exposed offspring, thus providing further insights into the unknown mechanisms underlying the in vivo effects of RF-EMF.

(NE) Sauter C, Dorn H, Bahr A, Hansen ML, Peter A, Bajbouj M, Danker-Hopfe H. Effects of exposure to electromagnetic fields emitted by GSM 900 and WCDMA mobile phones on cognitive function in young male subjects. Bioelectromagnetics. 32(3):179-190, 2011. (HU, BE)

Results of studies on the possible effects of electromagnetic fields emitted by mobile phones on cognitive functions are contradictory, therefore, possible effects of long-term (7 h 15 min) electromagnetic field (EMF) exposure to handset-like signals of Global System for Mobile Communications (GSM) 900 and Wideband Code-Division Multiple Access (WCDMA) on attention and working memory were studied. The sample comprised 30 healthy male subjects (mean ± SD: 25.3 ± 2.6 years), who were tested on nine study days in which they were exposed to three exposure conditions (sham, GSM 900 and WCDMA) in a randomly assigned and balanced order. All tests were presented twice (morning and afternoon) on each study day within a fixed timeframe. Univariate comparisons revealed significant changes when subjects were exposed to GSM 900 compared to sham, only in the vigilance test. In the WCDMA exposure condition, one parameter in the vigilance and one in the test on divided attention

were altered compared to sham. Performance in the selective attention test and the n-back task was not affected by GSM 900 or WCDMA exposure. Time-of-day effects were evident for the tests on divided and selective attention, as well as for working memory. After correction for multiple testing, only time-of-day effects remained significant in two tests, resulting in faster reactions in the afternoon trials. The results of the present study do not provide any evidence of an EMF effect on human cognition, but they underline the necessity to control for time of day.

(NE) Sauter C, Eggert T, Dorn H, Schmid G, Bolz T, Marasanov A, Hansen ML, Peter A, Danker-Hopfe H. Do signals of a hand-held TETRA transmitter affect cognitive performance, well-being, mood or somatic complaints in healthy young men? Results of a randomized double-blind cross-over provocation study. Environ Res. 140:85-94, 2015. (HU, BE)

BACKGROUND: TETRA (terrestrial trunked radio) is a digital radio communication standard, which has been implemented in several European countries and is used by public executives, transportation services, and by private companies. Studies on possible impacts on the users' health considering different exposure conditions are missing. OBJECTIVES: To investigate possible acute effects of electromagnetic fields (EMF) of two different levels of TETRA hand-held transmitter signals on cognitive function and well-being in healthy young males. METHODS: In the present double-blind cross-over study possible effects of short-term (2.5h) EMF exposure of handset-like signals of TETRA (385MHz) were studied in 30 healthy male participants (mean±SD: 25.4±2.6 years). Individuals were tested on nine study days, on which they were exposed to three different exposure conditions (Sham, TETRA 1.5W/kg and TETRA 6.0W/kg) in a randomly assigned and balanced order. Participants were tested in the afternoon at a fixed timeframe. RESULTS: Attention remained unchanged in two out of three tasks. In the working memory significant changes were observed in two out of four subtasks. Significant results were found in 5 out of 35 tested parameters, four of them led to an improvement in performance. Mood, well-being and subjective somatic complaints were not affected by TETRA exposure. CONCLUSIONS: The results of the present study do not indicate a negative impact of a short-term EMF-effect of TETRA on cognitive function and well-being in healthy young men.

(E) Schmid MR, Loughran SP, Regel SJ, Murbach M, Bratic Grunauer A, Rusterholz T, Bersagliere A, Kuster N, Achermann P. Sleep EEG alterations: effects of different pulse-modulated radio frequency electromagnetic fields. J Sleep Res. 21(1):50-58, 2012a. (HU, EE, BE, SL, WS)

Previous studies have observed increases in electroencephalographic power during sleep in the spindle frequency range (approximately 11-15 Hz) after exposure to mobile phone-like radio frequency electromagnetic fields (RF EMF). Results also suggest that pulse modulation of the signal is crucial to induce these effects. Nevertheless, it remains unclear which specific elements of the field are responsible for the observed changes. We investigated whether pulse-

modulation frequency components in the range of sleep spindles may be involved in mediating these effects. Thirty young healthy men were exposed, at weekly intervals, to three different conditions for 30 min directly prior to an 8-h sleep period. Exposure consisted of a 900-MHz RF EMF, pulse modulated at 14 Hz or 217 Hz, and a sham control condition. Both active conditions had a peak spatial specific absorption rate of 2 W kg(-1) . During exposure subjects performed three different cognitive tasks (measuring attention, reaction speed and working memory), which were presented in a fixed order. Electroencephalographic power in the spindle frequency range was increased during non-rapid eye movement sleep (2nd episode) following the 14-Hz pulse-modulated condition. A similar but non-significant increase was also observed following the 217-Hz pulse-modulated condition. Importantly, this exposure-induced effect showed considerable individual variability. Regarding cognitive performance, no clear exposure-related effects were seen. Consistent with previous findings, our results provide further evidence that pulse-modulated RF EMF alter brain physiology, although the time-course of the effect remains variable across studies. Additionally, we demonstrated that modulation frequency components within a physiological range may be sufficient to induce these effects.

(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, 2012b. (HU, EE, SL)

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 J, Stangassinger M. Nonthermal Effects of Lifelong High-Frequency Electromagnetic Field Exposure on Social Memory Performance in Rats. Behav Neurosci. 128:633-637, 2014. (AS, CE, BE, WS)

We are today surrounded almost constantly by high-frequency electromagnetic fields (EMFs) from mobile communications base stations. To date, however, there has been little concern regarding nonthermal effects of EMFs on cognition. In the present study, male and female rats were subjected to continuous far-field exposure to a frequency of 900-MHz (Global System for Mobile Communications [GSM]) or 1.966-GHz (Universal Mobile Telecommunications System [UMTS]) at 0.4 W/kg. Memory performance of adult EMF-exposed and sham-exposed female rats (at 6 months of age) and male rats (at 3 and 6 months of age) was tested using a social discrimination procedure. For this procedure, a target juvenile male was introduced to the subject's home cage for 4 min (Trial 1). After 30 min, the same target animal and a novel juvenile male were simultaneously presented to the subject for 4 min (Trial 2). Differences in sniffing duration to the familiar and novel target rats during Trial 2 were used to assess memory performance. EMF-exposed females exhibited no differences in sniffing duration compared with controls. In contrast, the sniffing durations of EMF-exposed males at 3 months of age were significantly affected. At 6 months of age, GSM-, but not UMTS-, exposed male adults showed a memory performance deficit. These findings provide new insight into the nonthermal effects of long-term high-frequency EMF exposure on memory.

(E) Schoeni A, Roser K, Röösli M. Memory performance, wireless communication and exposure to radiofrequency electromagnetic fields: A prospective cohort study in adolescents. Environ Int. 85:343-351, 2015. (HU, CE, BE)

BACKGROUND: The aim of this study is to investigate whether memory performance in adolescents is affected by radiofrequency electromagnetic fields (RF-EMF) from wireless device use or by the wireless device use itself due to non-radiation related factors in that context. METHODS: We conducted a prospective cohort study with 439 adolescents. Verbal and figural memory tasks at baseline and after one year were completed using a standardized, computerized cognitive test battery. Use of wireless devices was inquired by questionnaire and operator recorded mobile phone use data was obtained for a subgroup of 234 adolescents. RF-EMF dose measures considering various factors affecting RF-EMF exposure were computed for the brain and the whole body. Data were analysed using a longitudinal approach, to investigate whether cumulative exposure over one year was related to changes in memory performance. All analyses were adjusted for relevant confounders. RESULTS: The kappa coefficients between cumulative mobile phone call duration and RF-EMF brain and whole body dose were 0.62 and 0.67, respectively for the whole sample and 0.48 and 0.28, respectively for the sample with operator data. In linear exposure-response models an interquartile increase in cumulative operator recorded mobile phone call duration was associated with a decrease in figural memory performance score by -0.15 (95% CI: -0.33, 0.03) units. For cumulative RF-EMF brain and whole body dose corresponding decreases in figural memory scores were -0.26 (95% CI: -0.42, -0.10) and -0.40 (95% CI: -0.79, -0.01), respectively. No exposure-response associations were observed for sending text messages and duration of gaming, which produces tiny RF-EMF emissions. CONCLUSIONS: A change in memory performance over one year was negatively associated with cumulative duration of wireless phone use and more strongly with RF-EMF dose. This may indicate that RF-EMF exposure affects memory performance.

(E) Seckin E, Suren Basar F, Atmaca S, Kaymaz FF, Suzer A, Akar A, Sunan E, Koyuncu M.The effect of radiofrequency radiation generated by a Global System for Mobile Communications source on cochlear development in a rat model. J Laryngol Otol. 128:400-405, 2014. (AS, CE, CC, DE)

Objective: This study aimed to determine the effect of radiofrequency radiation generated by 900 and 1800 MHz Global System for Mobile Communications sources on cochlear development in the rat model. Methods: Eight pregnant albino Wistar rats were divided into three groups: control, 900 MHz and 1800 MHz. The latter two groups of pregnant rats were exposed to radiofrequency radiation for 1 hour per day starting on the 12th day of pregnancy until delivery. The rats in the control, 900 MHz and 1800 MHz groups gave birth to 24, 31 and 26 newborn rats respectively. Newborn rats in the 900 MHz and 1800 MHz groups were exposed to radiofrequency radiation for 1 hour per day for 21 days after delivery. Hearing evaluations of newborn rats were carried out using distortion product otoacoustic emissions testing. Eight newborn rats were randomly selected from each group for electron microscopic evaluation. Results: Distortion product otoacoustic emission tests revealed no significant difference among the groups, but electron microscopic evaluation revealed significant

differences among the groups with regard to the number of normal, apoptotic and necrotic cells. Conclusion: The findings indicated cellular structural damage in the cochlea caused by radiofrequency radiation exposure during cochlear development in the rat model.

(E) Sharma A, Sisodia R, Bhatnagar D, Saxena VK. Spatial memory and learning performance and its relationship to protein synthesis of Swiss albino mice exposed to 10 GHz microwaves. Int J Radiat Biol. 90:29-35, 2014. (AS, CE, BE, CH)

Purpose: To study the possible role of microwave (MW) exposure on spatial memory of Swiss albino mice and its relationship to protein concentration in whole brain. Materials and methods: Mice were exposed to 10 GHz (Giga Hertz) microwaves with the power density of 0.25 mW/cm^2 (milliwatt per centimeter square) with average whole body specific absorption rate (SAR) 0.1790 W/kg daily for 2 hours per day (h/day) for 30 days. After exposure mice were tested for spatial memory performance using Morris water maze test (MWT). For this purpose mice (6-8 weeks old) were divided into two groups (i) sham exposed and, (ii) microwaves exposed. After initial training for two days, MWT was performed for another 6 days. Protein was estimated 48 hours after exposure and immediately after completion of MWT. Results: Both sham exposed and microwave exposed animals showed a significant decrease in escape time with training. Microwave exposed animals had statistically significant higher mean latency to reach the target quadrant compared to sham exposed. A concurrent decrease in protein levels was estimated in whole brain of the exposed mice compared to sham exposed mice. Conclusions: It can be concluded from the current study that exposure to microwave radiation caused decrements in the ability of mice to learn the special memory task, this may be due to simultaneous decrease in protein levels in the brain of mice.

(E) Sharma A, Kesari KK, Saxena VK, Sisodia R. Ten gigahertz microwave radiation impairs spatial memory, enzymes activity, and histopathology of developing mice brain. Mol Cell Biochem. 2017 May 3. doi: 10.1007/s11010-017-3051-8. [Epub ahead of print] (AS, CE, BE, ME, OX)

For decades, there has been an increasing concern about the potential hazards of non-ionizing electromagnetic fields that are present in the environment and alarming as a major pollutant or electro-pollutant for health risk and neuronal diseases. Therefore, the objective of the present study was to explore the effects of 10 GHz microwave radiation on developing mice brain. Two weeks old mice were selected and divided into two groups (i) sham-exposed and (ii) microwave-exposed groups. Animals were exposed for 2 h/day for 15 consecutive days. After the completion of exposure, within an hour, half of the animals were autopsied immediately and others were allowed to attain 6 weeks of age for the follow-up study. Thereafter results were recorded in terms of various biochemical, behavioral, and histopathological parameters. Body weight result showed significant changes immediately after treatment, whereas non-significant changes were observed in mice attaining 6 weeks of age. Several other endpoints like brain weight, lipid peroxidation, glutathione, protein, catalase, and superoxide dismutase were also found significantly ($p < 0.05$) altered in mice whole brain. These significant differences were found immediately after exposure and also in follow-up on attaining 6 weeks of age in

microwave exposure group. Moreover, statistically significant ($p < 0.001$) effect was investigated in spatial memory of the animals, in learning to locate the position of platform in Morris water maze test. Although in probe trial test, sham-exposed animals spent more time in searching for platform into the target quadrant than in opposite or other quadrants. Significant alteration in histopathological parameters (qualitative and quantitative) was also observed in CA1 region of the hippocampus, cerebral cortex, and ansiform lobule of cerebellum. Results from the present study concludes that the brain of 2 weeks aged mice was very sensitive to microwave exposure as observed immediately after exposure and during follow-up study at 6 weeks of age.

(E) Shehu A, Mohammed A, Magaji RA, Muhammad MS. Exposure to mobile phone electromagnetic field radiation, ringtone and vibration affects anxiety-like behaviour and oxidative stress biomarkers in albino wistar rats. Metab Brain Dis. 31:355-362, 2016. (AS, CE, BE, OX)

Research on the effects of Mobile phone radio frequency emissions on biological systems has been focused on noise and vibrations as auditory stressors. This study investigated the potential effects of exposure to mobile phone electromagnetic field radiation, ringtone and vibration on anxiety-like behaviour and oxidative stress biomarkers in albino wistar rats. Twenty five male wistar rats were randomly divided into five groups of 5 animals each: group I: exposed to mobile phone in switched off mode (control), group II: exposed to mobile phone in silent mode, group III: exposed to mobile phone in vibration mode, group IV: exposed to mobile phone in ringtone mode, group V: exposed to mobile phone in vibration and ringtone mode. The animals in group II to V were exposed to 10 min call (30 missed calls for 20 s each) per day for 4 weeks. Neurobehavioural studies for assessing anxiety were carried out 24 h after the last exposure and the animals were sacrificed. Brain samples were collected for biochemical evaluation immediately. Results obtained showed a significant decrease ($P < 0.05$) in open arm duration in all the experimental groups when compared to the control. A significant decrease ($P < 0.05$) was also observed in catalase activity in group IV and V when compared to the control. In conclusion, the results of the present study indicates that 4 weeks exposure to electromagnetic radiation, vibration, ringtone or both produced a significant effect on anxiety-like behavior and oxidative stress in young wistar rats.

(NE) Shirai T, Imai N, Wang J, Takahashi S, Kawabe M, Wake K, Kawai H, Watanabe S-I, Furukawa F, Fujiwara O. Multigenerational effects of whole body exposure to 2.14 GHz W-CDMA cellular phone signals on brain function in rats. Bioelectromagnetics. 35(7):497-511, 2014. (AS, CE, BE, ME)

The present experimental study was carried out with rats to evaluate the effects of whole body exposure to 2.14 GHz band code division multiple access (W-CDMA) signals for 20 h a day, over three generations. The average specific absorption rate (SAR, in unit of W/kg) for dams was designed at three levels: high (<0.24 W/kg), low (<0.08 W/kg), and 0 (sham exposure). Pregnant mothers (4 rats/group) were exposed from gestational day (GD) 7 to weaning and then their

offspring (F_1 generation, 4 males and 4 females/dam, respectively) were continuously exposed until 6 weeks of age. The F_1 females were mated with F_1 males at 11 weeks old, and then starting from GD 7, they were exposed continuously to the electromagnetic field (EMF; one half of the F1 offspring was used for mating, that is, two of each sex per dam and 8 males and 8 females/group, except for all offspring for the functional development tests). This protocol was repeated in the same manner on pregnant F_2 females and F_3 pups; the latter were killed at 10 weeks of age. No abnormalities were observed in the mother rats (F_0, F_1, and F_2) and in the offspring (F_1, F_2, and F_3) in any biological parameters, including neurobehavioral function. Thus, it was concluded that under the experimental conditions applied, multigenerational whole body exposure to 2.14 GHz W-CDMA signals for 20 h/day did not cause any adverse effects on the F_1, F_2, and F_3 offspring.

(E) Sirav B, Seyhan N. Blood-brain barrier disruption by continuous-wave radio frequency radiation. Electromagn Biol Med. 28:215-222, 2009. (AS, ME)

The increasing use of cellular phones and the increasing number of associated base stations are becoming a widespread source of non ionizing electromagnetic radiation. Some biological effects are likely to occur even at low-level EM fields. This study was designed to investigate the effects of 900 and 1,800 MHz Continuous Wave Radio Frequency Radiation (CW RFR) on the permeability of Blood Brain Barrier (BBB) of rats. Results have shown that 20 min RFR exposure of 900 and 1,800 MHz induces an effect and increases the permeability of BBB of male rats. There was no change in female rats. The scientific evidence on RFR safety or harm remains inconclusive. More studies are needed to demonstrate the effects of RFR on the permeability of BBB and the mechanisms of that breakdown.

(E) Sirav B, Seyhan N. Effects of radiofrequency radiation exposure on blood-brain barrier permeability in male and female rats. Electromagn Biol Med. 30(4):253-260, 2011. (AS, ME)

During the last several decades, numerous studies have been performed aiming at the question of whether or not exposure to radiofrequency radiation (RFR) influences the permeability of the blood-brain barrier (BBB). The objective of this study was to investigate the effect of RFR on the permeability of BBB in male and female Wistar albino rats. Right brain, left brain, cerebellum, and total brain were analyzed separately in the study. Rats were exposed to 0.9 and 1.8 GHz continuous-wave (CW) RFR for 20 min (at SARs of 4.26 mW/kg and 1.46 mW/kg, respectively) while under anesthesia. Control rats were sham-exposed. Disruption of BBB integrity was detected spectrophotometrically using the Evans-blue dye, which has been used as a BBB tracer and is known to be bound to serum albumin. Right brain, left brain, cerebellum, and total brain were evaluated for BBB permeability. In female rats, no albumin extravasation was found in in the brain after RFR exposure. A significant increase in albumin was found in the brains of the RF-exposed male rats when compared to sham-exposed male brains. These results suggest that exposure to 0.9 and 1.8 GHz CW RFR at levels below the international limits can affect the vascular permeability in the brain of male rats. The possible risk of RFR exposure in humans is a major concern for the society. Thus, this topic should be investigated more thoroughly in the future.

(E) Sırav B, Seyhan N. Effects of GSM modulated radio-frequency electromagnetic radiation on permeability of blood-brain barrier in male & female rats. J Chem Neuroanat. 75(Pt B):123-127, 2016. (AS, ME)

With the increased use of mobile phones, their biological and health effects have become more important. Usage of mobile phones near the head increases the possibility of effects on brain tissue. This study was designed to investigate the possible effects of pulse modulated 900MHz and 1800MHz radio-frequency radiation on the permeability of blood-brain barrier of rats. Study was performed with 6 groups of young adult male and female wistar albino rats. The permeability of blood-brain barrier to intravenously injected evans blue dye was quantitatively examined for both control and radio-frequency radiation exposed groups. For male groups; Evans blue content in the whole brain was found to be 0.08±0.01mg% in the control, 0.13±0.03mg% in 900MHz exposed and 0.26±0.05mg% in 1800MHz exposed animals. In both male radio-frequency radiation exposed groups, the permeability of blood-brain barrier found to be increased with respect to the controls ($p<0.01$). 1800MHz pulse modulated radio-frequency radiation exposure was found more effective on the male animals ($p<0.01$). For female groups; dye contents in the whole brains were 0.14±0.01mg% in the control, 0.24±0.03mg% in 900MHz exposed and 0.14±0.02mg% in 1800MHz exposed animals. No statistical variance found between the control and 1800MHz exposed animals ($p>0.01$). However 900MHz pulse modulated radio-frequency exposure was found effective on the permeability of blood-brain barrier of female animals. Results have shown that 20min pulse modulated radio-frequency radiation exposure of 900MHz and 1800MHz induces an effect and increases the permeability of blood-brain barrier of male rats. For females, 900MHz was found effective and it could be concluded that this result may due to the physiological differences between female and male animals. The results of this study suggest that mobile phone radation could lead to increase the permeability of blood-brain barrier under non-thermal exposure levels. More studies are needed to demonstrate the mechanisms of that breakdown.

(E) Söderqvist F, Carlberg M, Hardell L. Mobile and cordless telephones, serum transthyretin and the blood-cerebrospinal fluid barrier: a cross-sectional study. Environ Health. 21; 8:19, 2009. (HU, PE)

BACKGROUND: Whether low-intensity radiofrequency radiation damages the blood-brain barrier has long been debated, but little or no consideration has been given to the blood-cerebrospinal fluid barrier. In this cross-sectional study we tested whether long-term and/or short-term use of wireless telephones was associated with changes in the serum transthyretin level, indicating altered transthyretin concentration in the cerebrospinal fluid, possibly reflecting an effect of radiation. **METHODS:** One thousand subjects, 500 of each sex aged 18-65 years, were randomly recruited using the population registry. Data on wireless telephone use were assessed by a postal questionnaire and blood samples were analyzed for serum transthyretin concentrations determined by standard immunonephelometric techniques on a BN Prospec instrument. **RESULTS:** The response rate was 31.4%. Logistic regression of dichotomized TTR serum levels with a cut-point of 0.31 g/l on wireless telephone use yielded increased odds ratios that were statistically not significant. Linear regression of time since first use overall and on the day that blood was withdrawn gave different results for males and females: for men significantly higher serum concentrations of TTR were seen the longer an analogue telephone or a mobile and cordless desktop telephone combined had been used, and in contrast, significantly lower serum levels were seen the longer an UMTS telephone had been

used. Adjustment for fractions of use of the different telephone types did not modify the effect for cumulative use or years since first use for mobile telephone and DECT, combined. For women, linear regression gave a significant association for short-term use of mobile and cordless telephones combined, indicating that the sooner blood was withdrawn after the most recent telephone call, the higher the expected transthyretin concentration. **CONCLUSION:** In this hypothesis-generating descriptive study time since first use of mobile telephones and DECT combined was significantly associated with higher TTR levels regardless of how much each telephone type had been used. Regarding short-term use, significantly higher TTR concentrations were seen in women the sooner blood was withdrawn after the most recent telephone call on that day.

(E) Söderqvist F, Carlberg M, Hansson Mild K, Hardell L. Exposure to an 890-MHz mobile phone-like signal and serum levels of S100B and transthyretin in volunteers. Toxicol Lett. 189(1):63-66, 2009. (HU, PE)

Whether low-intensity non-thermal microwave radiation alters the integrity of the blood-brain barrier has been debated since the late 1970s, yet no experimental study has been carried out on humans. The aim of this study was to test, using peripheral markers, whether exposure to a mobile phone-like signal alters the integrity of the human blood-brain and blood-cerebrospinal fluid barriers. A provocation study was carried out that exposed 41 volunteers to a 30 min GSM 890 MHz signal with an average specific energy absorption rate distribution of 1.0 W/kg in the temporal area of the head as measured over any 1g of contiguous tissue. The outcome was assessed by changes in serum concentrations of two putative markers of brain barrier integrity, S100B and transthyretin. Repeated blood sampling before and after the provocation showed no statistically significant increase in the serum levels of S100B, while for transthyretin a statistically significant increase was seen in the final blood sample 60 min after the end of the provocation as compared to the prior sample taken immediately after provocation (p=0.02). The clinical significance of this finding, if any, is unknown. Further randomized studies with use of additional more brain specific markers are needed.

(NE) Söderqvist F, Carlberg M, Hardell L. Use of wireless telephones and serum S100B levels: a descriptive cross-sectional study among healthy Swedish adults aged 18-65 years. Sci Total Environ. 407(2):798-805, 2009. (HU, PE)

BACKGROUND: Since the late 1970s, experimental animal studies have been carried out on the possible effects of low-intensive radiofrequency fields on the blood-brain barrier (BBB), but no epidemiological study has been published to date. **OBJECTIVE:** Using serum S100B as a putative marker of BBB dysfunction we performed a descriptive cross-sectional study to investigate whether protein levels were higher among frequent than non-frequent users of mobile and cordless desktop phones. **METHOD:** One thousand subjects, 500 of each sex aged 18-65 years, were randomly recruited using the population registry. Data on wireless phone use were assessed by a postal questionnaire and blood samples were analyzed for S100B. **RESULTS:** The response rate was 31.4%. The results from logistic and linear regression analyses were statistically insignificant, with one exception: the linear regression analysis of latency for UMTS

use, which after stratifying on gender remained significant only for men (p = 0.01; n = 31). A low p-value (0.052) was obtained for use of cordless phone (n = 98) prior to giving the blood samples indicating a weak negative association. Total use of mobile and cordless phones over time yielded odds ratio (OR) 0.8 and 95% confidence interval (CI) 0.3-2.0 and use on the same day as giving blood yielded OR=1.1, CI=0.4-2.8. **CONCLUSIONS:** This study failed to show that long- or short-term use of wireless telephones was associated with elevated levels of serum S100B as a marker of BBB integrity. The finding regarding latency of UMTS use may be interesting but it is based on small numbers. Generally, S100B levels were low and to determine whether this association - if causal - is clinically relevant, larger studies with sufficient follow-up are needed.

(E) Söderqvist F, Hardell L, Carlberg M, Mild KH. Radiofrequency fields, transthyretin, and Alzheimer's disease. J Alzheimers Dis. 20(2):599-606, 2010. (HU, PE, MA)

Radiofrequency field (RF) exposure provided cognitive benefits in an animal study. In Alzheimer's disease (AD) mice, exposure reduced brain amyloid-beta (Abeta) deposition through decreased aggregation of Abeta and increase in soluble Abeta levels. Based on our studies on humans on RF from wireless phones, we propose that transthyretin (TTR) might explain the findings. In a cross-sectional study on 313 subjects, we used serum TTR as a marker of cerebrospinal fluid TTR. We found a statistically significantly positive beta coefficient for TTR for time since first use of mobile phones and desktop cordless phones combined (P=0.03). The electromagnetic field parameters were similar for the phone types. In a provocation study on 41 persons exposed for 30 min to an 890-MHz GSM signal with specific absorption rate of 1.0 Watt/kg to the temporal area of the brain, we found statistically significantly increased serum TTR 60 min after exposure. In our cross-sectional study, use of oral snuff also yielded statistically significantly increased serum TTR concentrations and nicotine has been associated with decreased risk for AD and to upregulate the TTR gene in choroid plexus but not in the liver, another source of serum TTR. TTR sequesters Abeta, thereby preventing the formation of Abeta plaques in the brain. Studies have shown that patients with AD have lowered TTR concentrations in the cerebrospinal fluid and have attributed the onset of AD to insufficient sequestering of Abeta by TTR. We propose that TTR might be involved in the findings of RF exposure benefit in AD mice.

(E) Sokolovic D, Djindjic B, Nikolic J, Bjelakovic G, Pavlovic D, Kocic G, Krstic D, Cvetkovic T, Pavlovic V. Melatonin reduces oxidative stress induced by chronic exposure of microwave radiation from mobile phones in rat brain. J Radiat Res. 49(6):579-586, 2008. (AS, CE, CH, OX)

PURPOSE: The aim of the study was to evaluate the intensity of oxidative stress in the brain of animals chronically exposed to mobile phones and potential protective effects of melatonin in reducing oxidative stress and brain injury. **MATERIALS AND METHODS:** Experiments were performed on Wistar rats exposed to microwave radiation during 20, 40 and 60 days. Four groups were formed: I group (control)- animals treated by saline, intraperitoneally (i.p.) applied daily during follow up, II group (Mel)- rats treated daily with melatonin (2 mg kg(-1) body weight i.p.), III group (MWs)- microwave exposed rats, IV group (MWs + Mel)- MWs exposed

rats treated with melatonin (2 mg kg(-1) body weight i.p.). The microwave radiation was produced by a mobile test phone (SAR = 0.043-0.135 W/kg). **RESULTS:** A significant increase in the brain tissue malondialdehyde (MDA) and carbonyl group concentration was registered during exposure. Decreased activity of catalase (CAT) and increased activity of xanthine oxidase (XO) remained after 40 and 60 days of exposure to mobile phones. Melatonin treatment significantly prevented the increase in the MDA content and XO activity in the brain tissue after 40 days of exposure while it was unable to prevent the decrease of CAT activity and increase of carbonyl group contents. **CONCLUSION:** We demonstrated two important findings; that mobile phones caused oxidative damage biochemically by increasing the levels of MDA, carbonyl groups, XO activity and decreasing CAT activity; and that treatment with the melatonin significantly prevented oxidative damage in the brain.

(E) Sokolovic D, Djordjevic B, Kocic G, Babovic P, Ristic G, Stanojkovic Z, Sokolovic DM, Veljkovic A, Jankovic A, Radovanovic Z. The effect of melatonin on body mass and behaviour of rats during an exposure to microwave radiation from mobile phone. Bratisl Lek Listy. 113(5):265-269, 2012. (AS, CE, PE, BE)

BACKGROUND: Microwave radiation (MW) produced by wireless telecommunications and a number of electrical devices used in household or in healthcare institutions may cause various disorders in human organism. On the other hand, melatonin is a potent antioxidant, immunostimulator and neuromodulator. The aim of this research was to determine body mass and behaviour changes in rats after a chronic microwave exposure, as well as to determine the effects of melatonin on body mass and behaviour in irradiated rats. METHODS: Wistar rats were divided into the four experimental groups: I group (control) - rats treated with 0,9 % saline, II group (Mel) - rats treated with melatonin (2 mg/kg), III group (MW) - rats exposed to MW radiation (4 h/day), IV group (MW+Mel) - rats, which were both exposed to MW radiation and received melatonin premedication (2 mg/kg). RESULTS: A significant body mass reduction was noted in animals exposed to MW radiation when compared to controls after 20, 40 and 60 days ($p<0.001$). Furthermore, body weight was significantly increased ($p<0.05$) in irradiated rats, which received melatonin pretreatment (MW+Mel) in comparison to irradiated group (MW) after 20 days. Microwave radiation exposed animals showed an anxiety related behaviour (agitation, irritability) after 10 days of exposure. After the radiation source removal, changes in behaviour were less noticeable. Melatonin administration to irradiated rats caused a decrease in the stress induced behaviour. CONCLUSION: Microwave radiation causes body mass decrease and anxiety related behaviour in rats, however melatonin causes a reverse of those effects on both body weight and behaviour of irradiated animals (Fig. 2, Ref. 32).

(NE) Son Y, Jeong YJ, Kwon JH, Choi HD, Pack JK, Kim N, Lee YS, Lee HJ. 1950 MHz radiofrequency electromagnetic fields do not aggravate memory deficits in 5xFAD mice. Bioelectromagnetics. 37(6):391-399, 2016. (AS, CE, BE, CH)

The increased use of mobile phones has generated public concern about the impact of radiofrequency electromagnetic fields (RF-EMF) on health. In the present study, we investigated whether RF-EMFs induce molecular changes in amyloid precursor protein (APP)

processing and amyloid beta (Aβ)-related memory impairment in the 5xFAD mouse, which is a widely used amyloid animal model. The 5xFAD mice at the age of 1.5 months were assigned to two groups (RF-EMF- and sham-exposed groups, eight mice per group). The RF-EMF group was placed in a reverberation chamber and exposed to 1950 MHz electromagnetic fields for 3 months (SAR 5 W/kg, 2 h/day, 5 days/week). The Y-maze, Morris water maze, and novel object recognition memory test were used to evaluate spatial and non-spatial memory following 3-month RF-EMF exposure. Furthermore, Aβ deposition and APP and carboxyl-terminal fragment β (CTFβ) levels were evaluated in the hippocampus and cortex of 5xFAD mice, and plasma levels of Aβ peptides were also investigated. In behavioral tests, mice that were exposed to RF-EMF for 3 months did not exhibit differences in spatial and non-spatial memory compared to the sham-exposed group, and no apparent change was evident in locomotor activity. Consistent with behavioral data, RF-EMF did not alter APP and CTFβ levels or Aβ deposition in the brains of the 5xFAD mice. These findings indicate that 3-month RF-EMF exposure did not affect Aβ-related memory impairment or Aβ accumulation in the 5xFAD Alzheimer's disease model.

(E) Sonmez OF, Odaci E, Bas O, Kaplan S. Purkinje cell number decreases in the adult female rat cerebellum following exposure to 900 MHz electromagnetic field. Brain Res. 1356:95-101, 2010. (AS, CE, ME)

The biological effects of electromagnetic field (EMF) exposure from mobile phones have growing concern among scientists since there are some reports showing increased risk for human health, especially in the use of mobile phones for a long duration. In the presented study, the effects on the number of Purkinje cells in the cerebellum of 16-week (16 weeks) old female rats were investigated following exposure to 900 MHz EMF. Three groups of rats, a control group (CG), sham exposed group (SG) and an electromagnetic field exposed group (EMFG) were used in this study. While EMFG group rats were exposed to 900 MHz EMF (1h/day for 28 days) in an exposure tube, SG was placed in the exposure tube but not exposed to EMF (1h/day for 28 days). The specific energy absorption rate (SAR) varied between 0.016 (whole body) and 2 W/kg (locally in the head). The CG was not placed into the exposure tube nor was it exposed to EMF during the study period. At the end of the experiment, all of the female rats were sacrificed and the number of Purkinje cells was estimated using a stereological counting technique. Histopathological evaluations were also done on sections of the cerebellum. Results showed that the total number of Purkinje cells in the cerebellum of the EMFG was significantly lower than those of CG ($p<0.004$) and SG ($p<0.002$). In addition, there was no significant difference at the 0.05 level between the rats' body and brain weights in the EMFG and CG or SG. Therefore, it is suggested that long duration exposure to 900 MHz EMF leads to decreases of Purkinje cell numbers in the female rat cerebellum.

(E) Spichtig S, Scholkmann F, Chin L, Lehmann H, Wolf M. Assessment of intermittent UMTS electromagnetic field effects on blood circulation in the human auditory region using a near-infrared system. Bioelectromagnetics. 33(1):40-54, 2012. (HU, PE)

The aim of the present study was to assess the potential effects of intermittent Universal Mobile Telecommunications System electromagnetic fields (UMTS-EMF) on blood circulation in

the human head (auditory region) using near-infrared spectroscopy (NIRS) on two different timescales: short-term (effects occurring within 80 s) and medium-term (effects occurring within 80 s to 30 min). For the first time, we measured potential immediate effects of UMTS-EMF in real-time without any interference during exposure. Three different exposures (sham, 0.18 W/kg, and 1.8 W/kg) were applied in a controlled, randomized, crossover, and double-blind paradigm on 16 healthy volunteers. In addition to oxy-, deoxy-, and total haemoglobin concentrations ([O(2) Hb], [HHb], and [tHb], respectively), the heart rate (HR), subjective well-being, tiredness, and counting speed were recorded. During exposure to 0.18 W/kg, we found a significant short-term increase in Δ[O(2) Hb] and Δ[tHb], which is small (≈17%) compared to a functional brain activation. A significant decrease in the medium-term response of Δ[HHb] at 0.18 and 1.8 W/kg exposures was detected, which is in the range of physiological fluctuations. The medium-term ΔHR was significantly higher (+1.84 bpm) at 1.8 W/kg than for sham exposure. The other parameters showed no significant effects. Our results suggest that intermittent exposure to UMTS-EMF has small short- and medium-term effects on cerebral blood circulation and HR.

(NE) Stefanics G, Kellényi L, Molnár F, Kubinyi G, Thuróczy G, Hernádi I. Short GSM mobile phone exposure does not alter human auditory brainstem response. BMC Public Health. 7:325, 2007. (HU, EE)

BACKGROUND: There are about 1.6 billion GSM cellular phones in use throughout the world today. Numerous papers have reported various biological effects in humans exposed to electromagnetic fields emitted by mobile phones. The aim of the present study was to advance our understanding of potential adverse effects of the GSM mobile phones on the human hearing system. **METHODS:** Auditory Brainstem Response (ABR) was recorded with three non-polarizing Ag-AgCl scalp electrodes in thirty young and healthy volunteers (age 18-26 years) with normal hearing. ABR data were collected before, and immediately after a 10 minute exposure to 900 MHz pulsed electromagnetic field (EMF) emitted by a commercial Nokia 6310 mobile phone. Fifteen subjects were exposed to genuine EMF and fifteen to sham EMF in a double blind and counterbalanced order. Possible effects of irradiation was analyzed by comparing the latency of ABR waves I, III and V before and after genuine/sham EMF exposure. **RESULTS:** Paired sample t-test was conducted for statistical analysis. Results revealed no significant differences in the latency of ABR waves I, III and V before and after 10 minutes of genuine/sham EMF exposure. **CONCLUSION:** The present results suggest that, in our experimental conditions, a single 10 minute exposure of 900 MHz EMF emitted by a commercial mobile phone does not produce measurable immediate effects in the latency of auditory brainstem waves I, III and V.

(NE) Stefanics G, Thuróczy G, Kellényi L, Hernádi I. Effects of twenty-minute 3G mobile phone irradiation on event related potential components and early gamma synchronization in auditory oddball paradigm. Neuroscience. 157(2):453-462, 2008. (HU, EE)

We investigated the potential effects of 20 min irradiation from a new generation Universal Mobile Telecommunication System (UMTS) 3G mobile phone on human event related

potentials (ERPs) in an auditory oddball paradigm. In a double-blind task design, subjects were exposed to either genuine or sham irradiation in two separate sessions. Before and after irradiation subjects were presented with a random series of 50 ms tone burst (frequent standards: 1 kHz, P=0.8, rare deviants: 1.5 kHz, P=0.2) at a mean repetition rate of 1500 ms while electroencephalogram (EEG) was recorded. The subjects' task was to silently count the appearance of targets. The amplitude and latency of the N100, N200, P200 and P300 components for targets and standards were analyzed in 29 subjects. We found no significant effects of electromagnetic field (EMF) irradiation on the amplitude and latency of the above ERP components. In order to study possible effects of EMF on attentional processes, we applied a wavelet-based time-frequency method to analyze the early gamma component of brain responses to auditory stimuli. We found that the early evoked gamma activity was insensitive to UMTS RF exposition. Our results support the notion, that a single 20 min irradiation from new generation 3G mobile phones does not induce measurable changes in latency or amplitude of ERP components or in oscillatory gamma-band activity in an auditory oddball paradigm.

(NE) Stovner LJ, Oftedal G, Straume A, Johnsson A. Nocebo as headache trigger: evidence from a sham-controlled provocation study with RF fields. Acta Neurol Scand Suppl. 188:67-71, 2008. (HU, PE)

BACKGROUND: A large proportion of the population in Norway has experienced headache in connection with mobile phone use, but several double-blind provocation studies with radiofrequency (RF) and sham exposures have shown no relation between headache and mobile phone RF fields. AIMS: To investigate the type and location of headache experienced by participants in one provocation study in order to gain insight into possible causes and mechanisms of the headaches. METHOD: Questionnaire about headache, indication on figure of location of headache after exposure, interview with neurologist about headache features to make headache diagnoses. RESULTS: The 17 participants went through 130 trials (sham or RF exposure). No significant difference existed in headache type, laterality or location between the headaches experienced with the two exposures types. In most participants, the headache was compatible with tension-type headache. DISCUSSION: As participants experienced their typical 'mobile phone headache' both with and without RF exposure, and since the experiment did not involve the stress or the arm/head position of mobile phone use, the most likely explanation is that the headache in this situation is caused by negative expectations (nocebo). CONCLUSION: This and other similar studies indicate that headache occurring in connection with mobile phone use is not related to RF fields, and that a nocebo effect is important for this and possibly other headache triggers.

(E) **Sudan M, Kheifets L, Arah OA, Olsen J. Cell phone exposures and hearing loss in children in the Danish National Birth Cohort. Paediatr Perinat Epidemiol. 27(3):247-257, 2013. (HU, BE)**

BACKGROUND: Children today are exposed to cell phones early in life, and may be the most vulnerable if exposure is harmful to health. We investigated the association between cell phone use and hearing loss in children. METHODS: The Danish National Birth Cohort (DNBC) enrolled pregnant women between 1996 and 2002. Detailed interviews were conducted during

gestation, and when the children were 6 months, 18 months and 7 years of age. We used multivariable-adjusted logistic regression, marginal structural models (MSM) with inverse-probability weighting, and doubly robust estimation (DRE) to relate hearing loss at age 18 months to cell phone use at age 7 years, and to investigate cell phone use reported at age 7 in relation to hearing loss at age 7. RESULTS: Our analyses included data from 52 680 children. We observed weak associations between cell phone use and hearing loss at age 7, with odds ratios and 95% confidence intervals from the traditional logistic regression, MSM and DRE models being 1.21 [95% confidence interval [CI] 0.99, 1.46], 1.23 [95% CI 1.01, 1.49] and 1.22 [95% CI 1.00, 1.49], respectively. CONCLUSIONS: Our findings could have been affected by various biases and are not sufficient to conclude that cell phone exposures have an effect on hearing. This is the first large-scale epidemiologic study to investigate this potentially important association among children, and replication of these findings is needed.

(NE) Talebnejad MR, Sadeghi-Sarvestani A, Hossein Nowroozzadeh M, Mortazavi SMJ, Khalili MR. The effects of microwave radiation on rabbit's retina. Journal of Current Ophthalmology, Available online 9 October 2017. (AS, CE, EE, ME)

Purpose Mobile cell phones are used extensively these days, and their microwave (MW) radiation has been shown to affect the eye. The purpose of the present study was to evaluate the effects of MW radiation on rabbit retina. Methods This experimental study (concluded in 2015) was conducted on 40 adult white New Zealand rabbits. A Global System for Mobile Communications (GSM) cell phone simulator was used for MW irradiation. The rabbits were randomized into five groups (8 in each) and treated as follows: Group 1: no irradiation (sham); Group 2: irradiation at 10 cm for 1 day; Group 3: irradiation at 30 cm for 1 day; Group 4: irradiation at 10 cm for 3 days; and Group 5: irradiation at 30 cm for 3 days. Scotopic and photopic electroretinography (ERG) responses were obtained at baseline and 7 days after the last exposure. Then all the rabbits were euthanized, and their eyes were enucleated and sent for pathology examination. Kruskal–Wallis and Chi-Square tests were used to evaluate intergroup differences in ERG parameters and histological findings, respectively. Results ERG responses obtained 7 days after irradiation did not show any statistically significant difference between the groups ($P > 0.1$, for all tested parameters). There were statistically non-significant trends toward greater changes in the MW irradiated eyes. In pathological examination, retina was normal with no sign of degeneration or infiltration. Ciliary body congestion was observed in greater fraction of those who received higher MW doses. ($P = 0.005$).
Conclusions Histopathologically, cell phone simulated MW irradiation had no significant detrimental effect on the retina. However, ciliary body congestion was observed in greater fraction of those who received higher MW doses. Although there was no significant difference between post-treatment mean ERG values, there were statistically non-significant trends toward greater changes in the MW irradiated eyes. (E) **Tang J, Zhang Y, Yang L, Chen Q, Tan L, Zuo S, Feng H, Chen Z, Zhu G. Exposure to 900 MHz electromagnetic fields activates the mkp-1/ERK pathway and causes blood-brain barrier damage and cognitive impairment in rats. Brain Res. 1601:92-101, 2015. (AS, CE, BE, ME)**

With the rapid increase in the number of mobile phone users, the potential adverse effects of the electromagnetic field radiation emitted by a mobile phone has become a serious concern. This study demonstrated, for the first time, the blood-brain barrier and cognitive changes in rats exposed to 900MHz electromagnetic field (EMF) and aims to elucidate the potential molecular pathway underlying these changes. A total of 108 male Sprague-Dawley rats were exposed to a 900MHz, 1mW/cm^2 EMF or sham (unexposed) for 14 or 28 days (3h per day). The specific energy absorption rate (SAR) varied between 0.016 (whole body) and 2W/kg (locally in the head). In addition, the Morris water maze test was used to examine spatial memory performance determination. Morphological changes were investigated by examining ultrastructural changes in the hippocampus and cortex, and the Evans Blue assay was used to assess blood brain barrier (BBB) damage. Immunostaining was performed to identify heme oxygenase-1 (HO-1)-positive neurons and albumin extravasation detection. Western blot was used to determine HO-1 expression, phosphorylated ERK expression and the upstream mediator, mkp-1 expression. We found that the frequency of crossing platforms and the percentage of time spent in the target quadrant were lower in rats exposed to EMF for 28 days than in rats exposed to EMF for 14 days and unexposed rats. Moreover, 28 days of EMF exposure induced cellular edema and neuronal cell organelle degeneration in the rat. In addition, damaged BBB permeability, which resulted in albumin and HO-1 extravasation were observed in the hippocampus and cortex. Thus, for the first time, we found that EMF exposure for 28 days induced the expression of mkp-1, resulting in ERK dephosphorylation. Taken together, these results demonstrated that exposure to 900MHz EMF radiation for 28 days can significantly impair spatial memory and damage BBB permeability in rat by activating the mkp-1/ERK pathway.

(NE) Terao Y, Okano T, Furubayashi T, Yugeta A, Inomata-Terada S, Ugawa Y. Effects of thirty-minute mobile phone exposure on saccades. Clin Neurophysiol. 118(7):1545-1556, 2007. (HUPE)

OBJECTIVE: To investigate whether exposure to pulsed high-frequency electromagnetic field (pulsed EMF) emitted by a mobile phone has short-term effects on saccade performances. METHODS: A double blind, counterbalanced crossover design was employed. In 10 normal subjects, we studied the performance of visually guided saccade (VGS), gap saccade (GAP), and memory guided saccade (MGS) tasks before and after exposure to EMF emitted by a mobile phone for thirty minutes or sham exposure. We also implemented a hand reaction time (RT) task in response to a visual signal. RESULTS: With the exception of VGS and MGS latencies, the parameters of VGS, GAP and MGS tasks were unchanged before and after real or sham EMF exposure. In addition, the latencies of VGS and MGS did not change differently after real and sham exposure. The hand RT shortened with the repetition of trials, but again this trend was of similar magnitude for real and sham exposures. CONCLUSIONS: Thirty minutes of mobile phone exposure has no significant short-term effect on saccade performances. SIGNIFICANCE: This is the first study to investigate saccade performance in relation to mobile phone exposure. No significant effect of mobile phone use was demonstrated on the performance of various

saccade tasks, suggesting that the cortical processing for saccades and attention is not affected by exposure to EMF emitted by a mobile phone.

(NE) Thomas S, Benke G, Dimitriadis C, Inyang I, Sim MR, Wolfe R, Croft RJ, Abramson MJ. Use of mobile phones and changes in cognitive function in adolescents. Occup Environ Med. 67(12):861-866, 2010a. (HU, BE)

BACKGROUND: Several studies have investigated the impact of mobile phone exposure on cognitive function in adults. However, children and adolescents are of special interest due to their developing nervous systems. METHODS: Data were derived from the Australian Mobile Radiofrequency Phone Exposed Users' Study (MoRPhEUS) which comprised a baseline examination of year 7 students during 2005/2006 and a 1-year follow-up. Sociodemographic and exposure data were collected with a questionnaire. Cognitive functions were assessed with a computerised test battery and the Stroop Color-Word test. RESULTS: 236 students participated in both examinations. The proportion of mobile phone owners and the number of voice calls and short message services (SMS) per week increased from baseline to follow-up. Participants with more voice calls and SMS at baseline showed less reductions in response times over the 1-year period in various computerised tasks. Furthermore, those with increased voice calls and SMS exposure over the 1-year period showed changes in response time in a simple reaction and a working memory task. No associations were seen between mobile phone exposure and the Stroop test. CONCLUSIONS: We have observed that some changes in cognitive function, particularly in response time rather than accuracy, occurred with a latency period of 1 year and that some changes were associated with increased exposure. However, the increased exposure was mainly applied to those who had fewer voice calls and SMS at baseline, suggesting that these changes over time may relate to statistical regression to the mean, and not be the effect of mobile phone exposure.

(E) Thomas S, Heinrich S, von Kries R, Radon K. Exposure to radio-frequency electromagnetic fields and behavioural problems in Bavarian children and adolescents. Eur J Epidemiol. 25(2):135-141, 2010b. (HU, BE)

Only few studies have so far investigated possible health effects of radio-frequency electromagnetic fields (RF EMF) in children and adolescents, although experts discuss a potential higher vulnerability to such fields. We aimed to investigate a possible association between measured exposure to RF EMF fields and behavioural problems in children and adolescents. 1,498 children and 1,524 adolescents were randomly selected from the population registries of four Bavarian (South of Germany) cities. During an Interview data on participants' mental health, socio-demographic characteristics and potential confounders were collected. Mental health behaviour was assessed using the German version of the Strengths and Difficulties Questionnaire (SDQ). Using a personal dosimeter, we obtained radio-frequency EMF exposure profiles over 24 h. Exposure levels over waking hours were expressed as mean percentage of the reference level. Overall, exposure to radiofrequency electromagnetic fields was far below the reference level. Seven percent of the children and 5% of the adolescents showed an abnormal mental behaviour. In the multiple logistic regression analyses measured

exposure to RF fields in the highest quartile was associated to overall behavioural problems for adolescents (OR 2.2; 95% CI 1.1-4.5) but not for children (1.3; 0.7-2.6). These results are mainly driven by one subscale, as the results showed an association between exposure and conduct problems for adolescents (3.7; 1.6-8.4) and children (2.9; 1.4-5.9). As this is one of the first studies that investigated an association between exposure to mobile telecommunication networks and mental health behaviour more studies using personal dosimetry are warranted to confirm these findings.

(E) Thomée S, Härenstam A, Hagberg M. Mobile phone use and stress, sleep disturbances, and symptoms of depression among young adults--a prospective cohort study. BMC Public Health. 11:66, 2011. (HU, BE) (Effects may not be caused by RFR exposure.)

BACKGROUND: Because of the quick development and widespread use of mobile phones, and their vast effect on communication and interactions, it is important to study possible negative health effects of mobile phone exposure. The overall aim of this study was to investigate whether there are associations between psychosocial aspects of mobile phone use and mental health symptoms in a prospective cohort of young adults. METHODS: The study group consisted of young adults 20-24 years old (n = 4156), who responded to a questionnaire at baseline and 1-year follow-up. Mobile phone exposure variables included frequency of use, but also more qualitative variables: demands on availability, perceived stressfulness of accessibility, being awakened at night by the mobile phone, and personal overuse of the mobile phone. Mental health outcomes included current stress, sleep disorders, and symptoms of depression. Prevalence ratios (PRs) were calculated for cross-sectional and prospective associations between exposure variables and mental health outcomes for men and women separately. RESULTS: There were cross-sectional associations between high compared to low mobile phone use and stress, sleep disturbances, and symptoms of depression for the men and women. When excluding respondents reporting mental health symptoms at baseline, high mobile phone use was associated with sleep disturbances and symptoms of depression for the men and symptoms of depression for the women at 1-year follow-up. All qualitative variables had cross-sectional associations with mental health outcomes. In prospective analysis, overuse was associated with stress and sleep disturbances for women, and high accessibility stress was associated with stress, sleep disturbances, and symptoms of depression for both men and women. CONCLUSIONS: High frequency of mobile phone use at baseline was a risk factor for mental health outcomes at 1-year follow-up among the young adults. The risk for reporting mental health symptoms at follow-up was greatest among those who had perceived accessibility via mobile phones to be stressful. Public health prevention strategies focusing on attitudes could include information and advice, helping young adults to set limits for their own and others' accessibility.

(E) Tombini M, Pellegrino G, Pasqualetti P, Assenza G, Benvenga A, Fabrizio E, Rossini PM Mobile phone emissions modulate brain excitability in patients with focal epilepsy. Brain Stimul. 6:448-454, 2013. (HU, EE, MA)

BACKGROUND: Electromagnetic fields (EMFs) emitted by mobile phones had been shown to increase cortical excitability in healthy subjects following 45 min of continuous exposure on the ipsilateral hemisphere. OBJECTIVE: Using Transcranial Magnetic Stimulation (TMS), the current study assessed the effects of acute exposure to mobile phone EMFs on the cortical excitability in patients with focal epilepsy. METHODS: Ten patients with cryptogenic focal epilepsy originating outside the primary motor area (M1) were studied. Paired-pulse TMS were applied to the M1 of both the hemisphere ipsilateral (IH) and contralateral (CH) to the epileptic focus before and immediately after real/sham exposure to the GSM-EMFs (45 min). The TMS study was carried out in all subjects in three different experimental sessions (IH and CH exposure, sham), 1 week apart, according to a crossover, double-blind and counter-balanced paradigm. RESULTS: The present study clearly demonstrated that an acute and relatively prolonged exposure to GSM-EMFs modulates cortical excitability in patients affected by focal epilepsy; however, in contrast to healthy subjects, these effects were evident only after EMFs exposure over the hemisphere contralateral to the epileptic focus (CH). They were characterized by a significant cortical excitability increase in the exposed hemisphere paired with slight excitability decrease in the other one (IH). Both sham and real EMFs exposure of the IH did not affect brain excitability. CONCLUSION: Present results suggest a significant interaction between the brain excitability changes induced by EMFs and the epileptic focus, which eliminated the excitability enhancing effects of EMFs evident only in the CH.

(E) Tong J, Chen S, Liu XM, Hao DM. [Effect of electromagnetic radiation on discharge activity of neurons in the hippocampus CA1 in rats]. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 29(5):423-427, 2013. [Article in Chinese] (AS, CE, EE)

OBJECTIVE: In order to explore effect of electromagnetic radiation on learning and memory ability of hippocampus neuron in rats, the changes in discharge patterns and overall electrical activity of hippocampus neuron after electromagnetic radiation were observed. METHODS: Rat neurons discharge was recorded with glass electrode extracellular recording technology and a polygraph respectively. Radiation frequency of electromagnetic wave was 900 MHZ and the power was 10 W/m2. In glass electrode extracellular recording, the rats were separately irradiated for 10, 20, 30, 40, 50 and 60 min, every points repeated 10 times and updated interval of 1h, observing the changes in neuron discharge and spontaneous discharge patterns after electromagnetic radiation. In polygraph recording experiments, irradiation group rats for five days a week, 6 hours per day, repeatedly for 10 weeks, memory electrical changes in control group and irradiation group rats when they were feeding were repeatedly monitored by the implanted electrodes, observing the changes in peak electric digits and the largest amplitude in hippocampal CA1 area, and taking some electromagnetic radiation sampling sequence for correlation analysis. RESULTS: (1) Electromagnetic radiation had an inhibitory role on discharge frequency of the hippocampus CA1 region neurons. After electromagnetic radiation, discharge frequency of the hippocampus CA1 region neurons was reduced, but the changes in scale was not obvious. (2) Electromagnetic radiation might change the spontaneous discharge patterns of hippocampus CA1 region neurons, which made the explosive discharge pattern increased obviously. (3) Peak potential total number within 5 min in irradiation group

was significantly reduced, the largest amplitude was less than that of control group. (4) Using mathematical method to make the correlation analysis of the electromagnetic radiation sampling sequence, that of irradiation group was less than that of control group, indicating that there was a tending to be inhibitory connection between neurons in irradiation group after electromagnetic radiation. CONCLUSION: Electromagnetic radiation may cause structure and function changes of transfer synaptic in global, make hippocampal CA1 area neurons change in the overall discharge characteristic and discharge patterns, thus lead to decrease in the ability of learning and memory.

(E) Trosić I, Pavicić I, Milković-Kraus S, Mladinić M, Zeljezić D. Effect of electromagnetic radiofrequency radiation on the rats' brain, liver and kidney cells measured by comet assay. Coll Antropol. 35(4):1259-1264, 2011. (AS, CE, CH)

The goal of study was to evaluate DNA damage in rat's renal, liver and brain cells after in vivo exposure to radiofrequency/microwave (Rf/Mw) radiation of cellular phone frequencies range. To determine DNA damage, a single cell gel electrophoresis/comet assay was used. Wistar rats (male, 12 week old, approximate body weight 350 g) (N = 9) were exposed to the carrier frequency of 915 MHz with Global System Mobile signal modulation (GSM), power density of 2.4 W/m2, whole body average specific absorption rate SAR of 0.6 W/kg. The animals were irradiated for one hour/day, seven days/week during two weeks period. The exposure set-up was Gigahertz Transversal Electromagnetic Mode Cell (GTEM--cell). Sham irradiated controls (N = 9) were apart of the study. The body temperature was measured before and after exposure. There were no differences in temperature in between control and treated animals. Comet assay parameters such as the tail length and tail intensity were evaluated. In comparison with tail length in controls (13.5 +/- 0.7 microm), the tail was slightly elongated in brain cells of irradiated animals (14.0 +/- 0.3 microm). The tail length obtained for liver (14.5 +/- 0.3 microm) and kidney (13.9 +/- 0.5 microm) homogenates notably differs in comparison with matched sham controls (13.6 +/- 0.3 microm) and (12.9 +/- 0.9 microm). Differences in tail intensity between control and exposed animals were not significant. The results of this study suggest that, under the experimental conditions applied, repeated 915 MHz irradiation could be a cause of DNA breaks in renal and liver cells, but not affect the cell genome at the higher extent compared to the basal damage.

(NE) Trunk A, Stefanics G, Zentai N, Kovács-Bálint Z, Thuróczy G, Hernádi I. No effects of a single 3G UMTS mobile phone exposure on spontaneous EEG activity, ERP correlates, and automatic deviance detection. Bioelectromagnetics. 34: 31-42, 2013. (HU, EE)

Potential effects of a 30 min exposure to third generation (3G) Universal Mobile Telecommunications System (UMTS) mobile phone-like electromagnetic fields (EMFs) were investigated on human brain electrical activity in two experiments. In the first experiment, spontaneous electroencephalography (sEEG) was analyzed (n = 17); in the second experiment, auditory event-related potentials (ERPs) and automatic deviance detection processes reflected by mismatch negativity (MMN) were investigated in a passive oddball paradigm (n = 26). Both sEEG and ERP experiments followed a double-blind protocol where subjects were exposed to

either genuine or sham irradiation in two separate sessions. In both experiments, electroencephalograms (EEG) were recorded at midline electrode sites before and after exposure while subjects were watching a silent documentary. Spectral power of sEEG data was analyzed in the delta, theta, alpha, and beta frequency bands. In the ERP experiment, subjects were presented with a random series of standard (90%) and frequency-deviant (10%) tones in a passive binaural oddball paradigm. The amplitude and latency of the P50, N100, P200, MMN, and P3a components were analyzed. We found no measurable effects of a 30 min 3G mobile phone irradiation on the EEG spectral power in any frequency band studied. Also, we found no significant effects of EMF irradiation on the amplitude and latency of any of the ERP components. In summary, the present results do not support the notion that a 30 min unilateral 3G EMF exposure interferes with human sEEG activity, auditory evoked potentials or automatic deviance detection indexed by MMN.

(NE) Trunk A, Stefanics G, Zentai N, Bacskay I, Felinger A, Thuróczy G, Hernádi I. Lack of interaction between concurrent caffeine and mobile phone exposure on visual target detection: An ERP study. Pharmacol Biochem Behav. 124:412-420, 2014. (HU, BE, EE, IA)

BACKGROUND: Caffeine affects information processing by acting predominantly on cortical activation, arousal and attention. Millions consume caffeine and simultaneously use their mobile phone (MP) during everyday activities. However, it is not known whether and how MP-emitted electromagnetic fields (EMFs) can modulate known psychoactive effects of caffeine. Here we investigated behavioral and neural correlates of caffeine and simultaneous MP exposure in a third generation (3G) Universal Mobile Telecommunication System (UMTS) signal modulation scheme. METHODS: We recorded electroencephalography (EEG) and event related potentials (ERP) in an oddball paradigm to frequent standard (P=0.8) and rare target (P=0.2) stimuli in a placebo controlled, double blind, within-subject protocol in four experimental sessions: 1) no caffeine and no MP, 2) caffeine only, 3) MP only, 4) caffeine and MP. The subjects' task was to discriminate between standard and target stimuli and respond to the latter by pressing a button while reaction time (RT) and EEG were recorded. To provide a complete analysis of any possible caffeine and/or MP treatment effects that may have occurred, we analyzed the P300 ERP wave using four different ERP measures: 1) peak latency, 2) peak amplitude, 3) 50% fractional area latency (FAL) and 4) area under the curve (AUC). RESULTS: Caffeine significantly shortened RT and decreased AUC of the P300 component compared to the control or the UMTS MP alone conditions. However, no effects were observed on RT or P300 in the UMTS MP exposure sessions, neither alone nor in combination with caffeine. CONCLUSION: Overall, the present results did not demonstrate any interactive or synergistic effects of caffeine and UMTS MP like EMF exposure on basic neural or cognitive measures. However, we found that caffeine consistently enhanced behavioral and ERP measures of visual target detection, showing that present results were obtained using a pharmacologically validated, consistent and replicable methodology.

(NE) Trunk A, Stefanics G, Zentai N, Bacskay I, Felinger A, Thuróczy G, Hernádi I. Effects of concurrent caffeine and mobile phone exposure on local target probability processing in the human brain. Sci Rep. 5:14434, 2015. (HU, EE, BE)

Millions of people use mobile phones (MP) while drinking coffee or other caffeine containing beverages. Little is known about the potential combined effects of MP irradiation and caffeine on cognitive functions. Here we investigated whether caffeine intake and concurrent exposure to Universal Mobile Telecommunications System (UMTS) MP-like irradiation may interactively influence neuro-cognitive function in an active visual oddball paradigm. In a full factorial experimental design, 25 participants performed a simple visual target detection task while reaction time (RT) and electroencephalogram (EEG) was recorded. Target trials were divided into Low and High probability sets based on target-to-target distance. We analyzed single trial RT and alpha-band power (amplitude) in the pre-target interval. We found that RT was shorter in High vs. Low local probability trials, and caffeine further shortened RT in High probability trials relative to the baseline condition suggesting that caffeine improves the efficiency of implicit short-term memory. Caffeine also decreased pre-target alpha amplitude resulting in higher arousal level. Furthermore, pre-target gamma power positively correlated with RT, which may have facilitated target detection. However, in the present pharmacologically validated study UMTS exposure either alone or in combination with caffeine did not alter RT or pre-stimulus oscillatory brain activity.

(NE) Unterlechner M, Sauter C, Schmid G, Zeitlhofer J. No effect of an UMTS mobile phone-like electromagnetic field of 1.97 GHz on human attention and reaction time. Bioelectromagnetics. 29(2):145-153, 2008. (HU, BE)

Several studies in the past reported influences of electromagnetic emissions of GSM phones on reaction time in humans. However, there are currently only a few studies available dealing with possible effects of the electromagnetic fields emitted by UMTS mobile phones. In our study, 40 healthy volunteers (20 female, 20 male), aged 26.0 years (range 21-30 years) underwent four different computer tests measuring reaction time and attention under three different UMTS mobile phone-like exposure conditions (two exposure levels plus sham exposure). Exposure of the subjects was accomplished by small helical antennas operated close to the head and fed by a generic signal representing the emissions of a UMTS mobile phone under constant receiving conditions as well as under a condition of strongly varying transmit power. In the high exposure condition the resulting peak spatial average exposure of the test subjects in the cortex of the left temporal lobe of the brain was 0.63 W/kg (min. 0.25 W/kg, max. 1.49 W/kg) in terms of 1 g averaged SAR and 0.37 W/kg (min. 0.16 W/kg, max. 0.84 W/kg) in terms of 10 g averaged SAR, respectively. Low exposure condition was one-tenth of high exposure and sham was at least 50 dB below low exposure. Statistical analysis of the obtained test parameters showed that exposure to the generic UMTS signal had no statistically significant immediate effect on attention or reaction. Therefore, this study does not provide any evidence that exposure of UMTS mobiles interferes with attention under short-term exposure conditions.

(E) Vácha M, Puzová T, Kvícalová M. Radio frequency magnetic fields disrupt magnetoreception in American cockroach. J Exp Biol. 212(Pt 21):3473-3477, 2009. (AS, LI, BE)

The sense that allows birds to orient themselves by the Earth's magnetic field can be disabled by an oscillating magnetic field whose intensity is just a fraction of the geomagnetic field

intensity and whose oscillations fall into the medium or high frequency radio wave bands. This remarkable phenomenon points very clearly at one of two existing alternative magnetoreception mechanisms in terrestrial animals, i.e. the mechanism based on the radical pair reactions of specific photosensitive molecules. As the first such study in invertebrates, our work offers evidence that geomagnetic field reception in American cockroach is sensitive to a weak radio frequency field. Furthermore, we show that the 'deafening' effect at Larmor frequency 1.2 MHz is stronger than at different frequencies. The parameter studied was the rise in locomotor activity of cockroaches induced by periodic changes in the geomagnetic North positions by 60 deg. The onset of the disruptive effect of a 1.2 MHz field was found between 12 nT and 18 nT whereas the threshold of a doubled frequency field 2.4 MHz fell between 18 nT and 44 nT. A 7 MHz field showed no impact even in maximal 44 nT magnetic flux density. The results indicate resonance effects rather than non-specific bias of procedure itself and suggest that insects may be equipped with the same magnetoreception system as the birds.

(E) Varghese R, Majumdar A, Kumar G, Shukla A. Rats exposed to 2.45GHz of non-ionizing radiation exhibit behavioral changes with increased brain expression of apoptotic caspase 3. Pathophysiology. 2017 Nov 14. pii: S0928-4680(17)30052-4. doi: 10.1016/j.pathophys.2017.11.001. [Epub ahead of print] (AS, CE, BE, CH, OX)

In recent years there has been a tremendous increase in use of Wi-Fi devices along with mobile phones, globally. Wi-Fi devices make use of 2.4GHz frequency. The present study evaluated the impact of 2.45GHz radiation exposure for 4h/day for 45days on behavioral and oxidative stress parameters in female Sprague Dawley rats. Behavioral tests of anxiety, learning and memory were started from day 38. Oxidative stress parameters were estimated in brain homogenates after sacrificing the rats on day 45. In morris water maze, elevated plus maze and light dark box test, the 2.45GHz radiation exposed rats elicited memory decline and anxiety behavior. Exposure decreased activities of super oxide dismutase, catalase and reduced glutathione levels whereas increased levels of brain lipid peroxidation was encountered in the radiation exposed rats, showing compromised anti-oxidant defense. Expression of caspase 3 gene in brain samples were quantified which unraveled notable increase in the apoptotic marker caspase 3 in 2.45GHz radiation exposed group as compared to sham exposed group. No significant changes were observed in histopathological examinations and brain levels of TNF-α. Analysis of dendritic arborization of neurons showcased reduction in number of dendritic branching and intersections which corresponds to alteration in dendritic structure of neurons, affecting neuronal signaling. The study clearly indicates that exposure of rats to microwave radiation of 2.45GHz leads to detrimental changes in brain leading to lowering of learning and memory and expression of anxiety behavior in rats along with fall in brain antioxidant enzyme systems.

(E) Vecchio F, Babiloni C, Ferreri F, Curcio G, Fini R, Del Percio C, Rossini PM. Mobile phone emission modulates interhemispheric functional coupling of EEG alpha rhythms. Eur J Neurosci. 25(6):1908-1913, 2007. (HU, EE)

We tested the working hypothesis that electromagnetic fields from mobile phones (EMFs) affect interhemispheric synchronization of cerebral rhythms, an important physiological feature

of information transfer into the brain. Ten subjects underwent two electroencephalographic (EEG) recordings, separated by 1 week, following a crossover double-blind paradigm in which they were exposed to a mobile phone signal (global system for mobile communications; GSM). The mobile phone was held on the left side of the subject head by a modified helmet, and orientated in the normal position for use over the ear. The microphone was orientated towards the corner of the mouth, and the antenna was near the head in the parietotemporal area. In addition, we positioned another similar phone (but without battery) on the right side of the helmet, to balance the weight and to prevent the subject localizing the side of GSM stimulation (and consequently lateralizing attention). In one session the exposure was real (GSM) while in the other it was Sham; both sessions lasted 45 min. Functional interhemispheric connectivity was modelled using the analysis of EEG spectral coherence between frontal, central and parietal electrode pairs. Individual EEG rhythms of interest were delta (about 2-4 Hz), theta (about 4-6 Hz), alpha 1 (about 6-8 Hz), alpha 2 (about 8-10 Hz) and alpha 3 (about 10-12 Hz). Results showed that, compared to Sham stimulation, GSM stimulation modulated the interhemispheric frontal and temporal coherence at alpha 2 and alpha 3 bands. The present results suggest that prolonged mobile phone emission affects not only the cortical activity but also the spread of neural synchronization conveyed by interhemispherical functional coupling of EEG rhythms.

(E) Vecchio F, Babiloni C, Ferreri F, Buffo P, Cibelli G, Curcio G, van Dijkman S, Melgari JM, Giambattistelli F, Rossini PM. Mobile phone emission modulates inter-hemispheric functional coupling of EEG alpha rhythms in elderly compared to young subjects. Clin Neurophysiol. 121(2):163-171, 2010. (HU, EE, AD)

OBJECTIVE: It has been reported that GSM electromagnetic fields (GSM-EMFs) of mobile phones modulate--after a prolonged exposure--inter-hemispheric synchronization of temporal and frontal resting electroencephalographic (EEG) rhythms in normal young subjects [Vecchio et al., 2007]. Here we tested the hypothesis that this effect can vary on physiological aging as a sign of changes in the functional organization of cortical neural synchronization. **METHODS:** Eyes-closed resting EEG data were recorded in 16 healthy elderly subjects and 5 young subjects in the two conditions of the previous reference study. The GSM device was turned on (45 min) in one condition and was turned off (45 min) in the other condition. Spectral coherence evaluated the inter-hemispheric synchronization of EEG rhythms at the following bands: delta (about 2-4 Hz), theta (about 4-6 Hz), alpha 1 (about 6-8 Hz), alpha 2 (about 8-10 Hz), and alpha 3 (about 10-12 Hz). The aging effects were investigated comparing the inter-hemispheric EEG coherence in the elderly subjects vs. a young group formed by 15 young subjects (10 young subjects of the reference study; Vecchio et al., 2007). **RESULTS:** Compared with the young subjects, the elderly subjects showed a statistically significant ($p<0.001$) increment of the inter-hemispheric coherence of frontal and temporal alpha rhythms (about 8-12 Hz) during the GSM condition. **CONCLUSIONS:** These results suggest that GSM-EMFs of a mobile phone affect inter-hemispheric synchronization of the dominant (alpha) EEG rhythms as a function of the physiological aging. **SIGNIFICANCE:** This study provides further evidence that physiological aging is related to changes in the functional organization of cortical neural synchronization.

(E) Vecchio F, Buffo P, Sergio S, Iacoviello D, Rossini PM, Babiloni C. Mobile phone emission modulates event-related desynchronization of α rhythms and cognitive-motor performance in healthy humans. Clin Neurophysiol. 123(1):121-128, 2012a. (HU, EE, BE)

OBJECTIVES: It has been shown that electromagnetic fields of Global System for Mobile Communications phone (GSM-EMFs) affect human brain rhythms (Vecchio et al., 2007, 2010), but it is not yet clear whether these effects are related to alterations of cognitive functions. **METHODS:** Eleven healthy adults underwent two electroencephalographic (EEG) sessions separated by 1 week, following a cross-over, placebo-controlled, double-blind paradigm. In both sessions, they performed a visual go/no-go task before real exposure to GSM-EMFs or after a sham condition with no EMF exposure. In the GSM real session, temporal cortex was continuously exposed to GSM-EMFs for 45 min. In the sham session, the subjects were not aware that the EMFs had been switched off for the duration of the experiment. In the go/no-go task, a central fixation stimulus was followed by a green (50% of probability) or red visual stimulus. Subjects had to press the mouse button after the green stimuli (go trials). With reference to a baseline period, power decrease of low- (about 8-10 Hz) and high-frequency (about 10-12 Hz) alpha rhythms indexed the cortical activity. **RESULTS:** It was found less power decrease of widely distributed high-frequency alpha rhythms and faster reaction time to go stimuli in the post- than pre-exposure period of the GSM session. No effect was found in the sham session. **CONCLUSIONS:** These results suggest that the peak amplitude of alpha ERD and the reaction time to the go stimuli are modulated by the effect of the GSM-EMFs on the cortical activity. **SIGNIFICANCE:** Exposure to GSM-EMFs for 45 min may enhance human cortical neural efficiency and simple cognitive-motor processes in healthy adults.

(E) Vecchio F, Tombini M, Buffo P, Assenza G, Pellegrino G, Benvenga A, Babiloni C, Rossini PM. Mobile phone emission increases inter-hemispheric functional coupling of electroencephalographic alpha rhythms in epileptic patients. Int J Psychophysiol. 84(2):164-171, 2012b. (HU, EE, MA)

It has been reported that GSM electromagnetic fields (GSM-EMFs) of mobile phones modulate - after a prolonged exposure - inter-hemispheric synchronization of temporal and frontal resting electroencephalographic (EEG) rhythms in normal young and elderly subjects (Vecchio et al., 2007, 2010). Here we tested the hypothesis that this can be even more evident in epileptic patients, who typically suffer from abnormal mechanisms governing synchronization of rhythmic firing of cortical neurons. Eyes-closed resting EEG data were recorded in ten patients affected by focal epilepsy in real and sham exposure conditions. These data were compared with those obtained from 15 age-matched normal subjects of the previous reference studies. The GSM device was turned on (45 min) in the "GSM" condition and was turned off (45 min) in the other condition ("sham"). The mobile phone was always positioned on the left side in both patients and control subjects. Spectral coherence evaluated the inter-hemispheric synchronization of EEG rhythms at the following frequency bands: delta (about 2-4 Hz), theta (about 4-6 Hz), alpha1 (about 6-8 Hz), alpha2 (about 8-10 Hz), and alpha3 (about 10-12 Hz). The effects on the patients were investigated comparing the inter-hemispheric EEG coherence in the epileptic patients with the control group of subjects evaluated in the previous reference

studies. Compared with the control subjects, epileptic patients showed a statistically significant higher inter-hemispheric coherence of temporal and frontal alpha rhythms (about 8-12 Hz) in the GSM than "Sham" condition. These results suggest that GSM-EMFs of mobile phone may affect inter-hemispheric synchronization of the dominant (alpha) EEG rhythms in epileptic patients. If confirmed by future studies on a larger group of epilepsy patients, the modulation of the inter-hemispheric alpha coherence due to the GSM-EMFs could have clinical implications and be related to changes in cognitive-motor function.

(E) Vecsei Z, Csathó A, Thuróczy G, Hernádi I. Effect of a single 30 min UMTS mobile phone**-like exposure on the thermal pain threshold of young healthy volunteers. Bioelectromagnetics. 34:530-541, 2013. (HU, BE)**

One of the most frequently investigated effects of radiofrequency electromagnetic fields (RF EMFs) on the behavior of complex biological systems is pain sensitivity. Despite the growing body of evidence of EMF-induced changes in pain sensation, there is no currently accepted experimental protocol for such provocation studies for the healthy human population. In the present study, therefore, we tested the effects of third generation Universal Mobile Telecommunications System (UMTS) RF EMF exposure on the thermal pain threshold (TPT) measured on the surface of the fingers of 20 young adult volunteers. The protocol was initially validated with a topical capsaicin treatment. The exposure time was 30 min and the genuine (or sham) signal was applied to the head through a patch antenna, where RF EMF specific absorption rate (SAR) values were controlled and kept constant at a level of 1.75 W/kg. Data were obtained using randomized, placebo-controlled trials in a double-blind manner. Subjective pain ratings were tested blockwise on a visual analogue rating scale (VAS). Compared to the control and sham conditions, the results provide evidence for intact TPT but a reduced desensitization effect between repeated stimulations within the individual blocks of trials, observable only on the contralateral side for the genuine UMTS exposure. Subjective pain perception (VAS) data indicated marginally decreased overall pain ratings in the genuine exposure condition only. The present results provide pioneering information about human pain sensation in relation to RF EMF exposure and thus may contribute to cover the existing gap between safety research and applied biomedical science targeting the potential biological effects of environmental RF EMFs.

(E) Velayutham P, Govindasamy GK, Raman R, Prepageran N, Ng KH. High-frequency hearing loss among mobile phone users. Indian J Otolaryngol Head Neck Surg. 66(Suppl 1):169-172, 2014. doi: (HU, BE)

The objective of this study is to assess high frequency hearing (above 8 kHz) loss among prolonged mobile phone users is a tertiary Referral Center. Prospective single blinded study. This is the first study that used high-frequency audiometry. The wide usage of mobile phone is so profound that we were unable to find enough non-users as a control group. Therefore we compared the non-dominant ear to the dominant ear using audiometric measurements. The study was a blinded study wherein the audiologist did not know which was the dominant ear. A total of 100 subjects were studied. Of the

subjects studied 53% were males and 47% females. Mean age was 27. The left ear was dominant in 63%, 22% were dominant in the right ear and 15% did not have a preference. This study showed that there is significant loss in the dominant ear compared to the non-dominant ear ($P < 0.05$). Chronic usage mobile phone revealed high frequency hearing loss in the dominant ear (mobile phone used) compared to the non dominant ear.

(E) Volkow ND, Tomasi D, Wang GJ, Vaska P, Fowler JS, Telang F, Alexoff D, Logan J, Wong C. Effects of cell phone radiofrequency signal exposure on brain glucose metabolism. JAMA. 305(8):808-813, 2011. (HU, PE)

CONTEXT: The dramatic increase in use of cellular telephones has generated concern about possible negative effects of radiofrequency signals delivered to the brain. However, whether acute cell phone exposure affects the human brain is unclear. **OBJECTIVE:** To evaluate if acute cell phone exposure affects brain glucose metabolism, a marker of brain activity. **DESIGN, SETTING, AND PARTICIPANTS:** Randomized crossover study conducted between January 1 and December 31, 2009, at a single US laboratory among 47 healthy participants recruited from the community. Cell phones were placed on the left and right ears and positron emission tomography with ((18)F)fluorodeoxyglucose injection was used to measure brain glucose metabolism twice, once with the right cell phone activated (sound muted) for 50 minutes ("on" condition) and once with both cell phones deactivated ("off" condition). Statistical parametric mapping was used to compare metabolism between on and off conditions using paired t tests, and Pearson linear correlations were used to verify the association of metabolism and estimated amplitude of radiofrequency-modulated electromagnetic waves emitted by the cell phone. Clusters with at least 1000 voxels (volume >8 cm(3)) and $P < .05$ (corrected for multiple comparisons) were considered significant. **MAIN OUTCOME MEASURE:** Brain glucose metabolism computed as absolute metabolism (µmol/100 g per minute) and as normalized metabolism (region/whole brain). **RESULTS:** Whole-brain metabolism did not differ between on and off conditions. In contrast, metabolism in the region closest to the antenna (orbitofrontal cortex and temporal pole) was significantly higher for on than off conditions (35.7 vs 33.3 µmol/100 g per minute; mean difference, 2.4 [95% confidence interval, 0.67-4.2]; $P = .004$). The increases were significantly correlated with the estimated electromagnetic field amplitudes both for absolute metabolism ($R = 0.95$, $P < .001$) and normalized metabolism ($R = 0.89$; $P < .001$). **CONCLUSIONS:** In healthy participants and compared with no exposure, 50-minute cell phone exposure was associated with increased brain glucose metabolism in the region closest to the antenna. This finding is of unknown clinical significance.

(NE) Wallace D, Eltiti S, Ridgewell A, Garner K, Russo R, Sepulveda F, Walker S, Quinlan T, Dudley S, Maung S, Deeble R, Fox E. Cognitive and physiological responses in humans exposed to a TETRA base station signal in relation to perceived electromagnetic hypersensitivity. Bioelectromagnetics. 33(1):23-39, 2012. (HU, BE)

Terrestrial Trunked Radio (TETRA) technology ("Airwave") has led to public concern because of its potential interference with electrical activity in the brain. The present study is the first to examine whether acute exposure to a TETRA base station signal has an impact on cognitive

functioning and physiological responses. Participants were exposed to a 420 MHz TETRA signal at a power flux density of 10 mW/m(2) as well as sham (no signal) under double-blind conditions. Fifty-one people who reported a perceived sensitivity to electromagnetic fields as well as 132 controls participated in a double-blind provocation study. Forty-eight sensitive and 132 control participants completed all three sessions. Measures of short-term memory, working memory, and attention were administered while physiological responses (blood volume pulse, heart rate, skin conductance) were monitored. After applying exclusion criteria based on task performance for each aforementioned cognitive measure, data were analyzed for 36, 43, and 48 sensitive participants for these respective tasks and, likewise, 107,125, and 129 controls. We observed no differences in cognitive performance between sham and TETRA exposure in either group; physiological response also did not differ between the exposure conditions. These findings are similar to previous double-blind studies with other mobile phone signals (900-2100 MHz), which could not establish any clear evidence that mobile phone signals affect health or cognitive function.

(E) Wang H, Peng R, Zhou H, Wang S, Gao Y, Wang L, Yong Z, Zuo H, Zhao L, Dong J, Xu X, Su Z. Impairment of long-term potentiation induction is essential for the disruption of spatial memory after microwave exposure. Int J Radiat Biol. 89:1100-1107, 2013. (AS, BE, ME, EE)

Purpose: To assess the impact of microwave exposure on learning and memory and to explore the underlying mechanisms. Materials and methods: 100 Wistar rats were exposed to a 2.856 GHz pulsed microwave field at average power densities of 0 mW/cm^2, 5 mW/cm^2, 10 mW/cm^2 and 50 mW/cm^2 for 6 min. The spatial memory was assessed by the Morris Water Maze (MWM) task. An in vivo study was conducted soon after microwave exposure to evaluate the changes of population spike (PS) amplitudes of long-term potentiation (LTP) in the medial perforant path (MPP)-dentate gyrus (DG) pathway. The structure of the hippocampus was observed by the light microscopy and the transmission electron microscopy (TEM) at 7 d after microwave exposure. Results: Our results showed that the rats exposed in 10 mW/cm^2 and 50 mW/cm^2 microwave displayed significant deficits in spatial learning and memory at 6 h, 1 d and 3 d after exposure. Decreased PS amplitudes were also found after 10 mW/cm^2 and 50 mW/cm^2 microwave exposure. In addition, varying degrees of degeneration of hippocampal neurons, decreased synaptic vesicles and blurred synaptic clefts were observed in the rats exposed in 10 mW/cm^2 and 50 mW/cm^2 microwave. Compared with the sham group, the rats exposed in 5 mW/cm^2 microwave showed no difference in the above experiments. Conclusions: This study suggested that impairment of LTP induction and the damages of hippocampal structure, especially changes of synapses, might contribute to cognitive impairment after microwave exposure.

(E) Wang H, Peng R, Zhao L, Wang S, Gao Y, Wang L, Zuo H, Dong J, Xu X, Zhou H, Su Z. The relationship between NMDA receptors and microwave induced learning and memory impairment: a long term observation on Wistar rats. Int J Radiat Biol. 91:262-269, 2015. (AS, BE, ME, CH)

Purpose: In the present study, we intended to investigate whether the high power microwave could cause the continuous disorders of learning and memory in Wistar rats and to explore the underlying mechanisms. Materials and methods: 80 Wistar rats were exposed to a 2.856 GHz pulsed microwave source at a power density of 0 mW/cm^2 and 50 mW/cm^2 microwave for 6 min. The spatial memory ability, the structure of the hippocampus, contents of amino acids neurotransmitters in hippocampus and the expression of N-methyl-D-aspartic acid receptors (NMDAR) subunit 1, 2A and 2B (NR1, NR2A and NR2B) were detected at 1 m, 3 m, 6 m, 9 m, 12 m and 18 m after microwave exposure. Results: Our results showed that the microwave exposed rats showed consistent deficiencies in spatial learning and memory. The level of amino acid neurotransmitters also decreased after microwave radiation. The ratio of glutamate (Glu) and gamma-aminobutyric acid (GABA) significantly decreased at 6 m. Besides, the hippocampus showed varying degrees of degeneration of neurons, increased postsynaptic density and blurred synaptic clefts in the exposure group. The NR1 and NR2B expression showed a significant decrease, especially the NR2B expression. Conclusions: This study indicated that the content of amino acids neurotransmitters, the expression of NMDAR subunits and the variation of hippocampal structure might contribute to the long term cognitive impairment after microwave exposure.

(E) Wang H, Tan S, Xu X, Zhao L, Zhang J, Yao B, Gao Y, Zhou H, Peng R. Long term impairment of cognitive functions and alterations of NMDAR subunits after continuous microwave exposure. Physiol Behav. 181:1-9, 2017. (AS, CE, BE, ME, EE)

OBJECTIVE: The long term effects of continuous microwave exposure cannot be ignored for the simulation of the real environment and increasing concerns about the negative cognitive effects of microwave exposure. METHODS: In this study, 220 male Wistar rats were exposed by a 2.856GHz radiation source with the average power density of 0, 2.5, 5 and 10mW/cm^2 for 6min/day, 5days/week and up to 6weeks. The MWM task, the EEG analysis, the hippocampus structure observation and the western blot were applied until the 12months after microwave exposure to detect the spatial learning and memory abilities, the cortical electrical activity, changes of hippocampal structure and the NMDAR subunits expressions. RESULTS: Results found that the rats in the 10mW/cm^2 group showed the decline of spatial learning and memory abilities and EEG disorders (the decrease of EEG frequencies, and increase of EEG amplitudes and delta wave powers). Moreover, changes of basic structure and ultrastructure of hippocampus also found in the 10 and 5mW/cm^2 groups. The decrease of NR 2A, 2B and p-NR2B might contribute to the impairment of cognitive functions. CONCLUSIONS: Our findings suggested that the continuous microwave exposure could cause the dose-dependent long term impairment of spatial learning and memory, the abnormalities of EEG and the hippocampal structure injuries. The decrease of NMDAR key subunits and phosphorylation of NR 2B might contribute to the cognitive impairment.

(E) Wang K, Lu JM, Xing ZH, Zhao QR, Hu LQ, Xue L, Zhang J, Mei YA. Effect of 1.8 GHz radiofrequency electromagnetic radiation on novel object associative recognition memory in mice. Sci Rep. 7:44521, 2017. (AS, BE, CC, ME)

Mounting evidence suggests that exposure to radiofrequency electromagnetic radiation (RF-

EMR) can influence learning and memory in rodents. In this study, we examined the effects of single exposure to 1.8 GHz RF-EMR for 30 min on subsequent recognition memory in mice, using the novel object recognition task (NORT). RF-EMR exposure at an intensity of >2.2 W/kg specific absorption rate (SAR) power density induced a significant density-dependent increase in NORT index with no corresponding changes in spontaneous locomotor activity. RF-EMR exposure increased dendritic-spine density and length in hippocampal and prefrontal cortical neurons, as shown by Golgi staining. Whole-cell recordings in acute hippocampal and medial prefrontal cortical slices showed that RF-EMR exposure significantly altered the resting membrane potential and action potential frequency, and reduced the action potential half-width, threshold, and onset delay in pyramidal neurons. These results demonstrate that exposure to 1.8 GHz RF-EMR for 30 min can significantly increase recognition memory in mice, and can change dendritic-spine morphology and neuronal excitability in the hippocampus and prefrontal cortex. The SAR in this study (3.3 W/kg) was outside the range encountered in normal daily life, and its relevance as a potential therapeutic approach for disorders associated with recognition memory deficits remains to be clarified.

(E) Wang LF, Li X, Gao YB, Wang SM, Zhao L, Dong J, Yao BW, Xu XP, Chang GM, Zhou HM, Hu XJ, Peng RY. Activation of VEGF/Flk-1-ERK Pathway Induced Blood-Brain Barrier Injury After Microwave Exposure. Mol Neurobiol. 52:478-491, 2015. (CS, ME, CH)

Microwaves have been suggested to induce neuronal injury and increase permeability of the blood-brain barrier (BBB), but the mechanism remains unknown. The role of the vascular endothelial growth factor (VEGF)/Flk-1-Raf/MAPK kinase (MEK)/extracellular-regulated protein kinase (ERK) pathway in structural and functional injury of the blood-brain barrier (BBB) following microwave exposure was examined. An in vitro BBB model composed of the ECV304 cell line and primary rat cerebral astrocytes was exposed to microwave radiation (50 mW/cm2, 5 min). The structure was observed by scanning electron microscopy (SEM) and the permeability was assessed by measuring transendothelial electrical resistance (TEER) and horseradish peroxidase (HRP) transmission. Activity and expression of VEGF/Flk-1-ERK pathway components and occludin also were examined. Our results showed that microwave radiation caused intercellular tight junctions to broaden and fracture with decreased TEER values and increased HRP permeability. After microwave exposure, activation of the VEGF/Flk-1-ERK pathway and Tyr phosphorylation of occludin were observed, along with down-regulated expression and interaction of occludin with zonula occludens-1 (ZO-1). After Flk-1 (SU5416) and MEK1/2 (U0126) inhibitors were used, the structure and function of the BBB were recovered. The increase in expression of ERK signal transduction molecules was muted, while the expression and the activity of occludin were accelerated, as well as the interactions of occludin with p-ERK and ZO-1 following microwave radiation. Thus, microwave radiation may induce BBB damage by activating the VEGF/Flk-1-ERK pathway, enhancing Tyr phosphorylation of occludin, while partially inhibiting expression and interaction of occludin with ZO-1.

(E) Wang LF, Tian DW, Li HJ, Gao YB, Wang CZ, Zhao L, Zuo HY, Dong J, Qiao SM, Zou Y, Xiong L, Zhou HM, Yang YF, Peng RY, Hu XJ. Identification of a Novel Rat NR2B Subunit Gene Promoter Region Variant and Its Association with Microwave-Induced Neuron Impairment. Mol Neurobiol. 53(4):2100-2111, 2016. (AS, CE, CH, BE)

Microwave radiation has been implicated in cognitive dysfunction and neuronal injury in animal models and in human investigations; however, the mechanism of these effects is unclear. In this study, single nucleotide polymorphism (SNP) sites in the rat GRIN2B promoter region were screened. The associations of these SNPs with microwave-induced rat brain dysfunction and with rat pheochromocytoma-12 (PC12) cell function were investigated. Wistar rats (n = 160) were exposed to microwave radiation (30 mW/cm(2) for 5 min/day, 5 days/week, over a period of 2 months). Screening of the GRIN2B promoter region revealed a stable C-to-T variant at nucleotide position -217 that was not induced by microwave exposure. The learning and memory ability, amino acid contents in the hippocampus and cerebrospinal fluid, and NR2B expression were then investigated in the different genotypes. Following microwave exposure, NR2B protein expression decreased, while the Glu contents in the hippocampus and CSF increased, and memory impairment was observed in the TT genotype but not the CC and CT genotypes. In PC12 cells, the effects of the T allele were more pronounced than those of the C allele on transcription factor binding ability, transcriptional activity, NR2B mRNA, and protein expression. These effects may be related to the detrimental role of the T allele and the protective role of the C allele in rat brain function and PC12 cells exposed to microwave radiation.

(NE) Watilliaux A, Edeline JM, Lévêque P, Jay TM, Mallat M. Effect of exposure to 1,800 MHz electromagnetic fields on heat shock proteins and glial cells in the brain of developing rats. Neurotox Res. 20(2):109-119, 2011. (AS, DE, CC)

The increasing use of mobile phones by children raise issues about the effects of electromagnetic fields (EMF) on the immature Central Nervous System (CNS). In the present study, we quantified cell stress and glial responses in the brain of developing rats one day after a single exposure of 2 h to a GSM 1,800 MHz signal at a brain average Specific Absorption Rate (SAR) in the range of 1.7 to 2.5 W/kg. Young rats, exposed to EMF on postnatal days (P) 5 (n = 6), 15 (n = 5) or 35 (n = 6), were compared to pseudo-exposed littermate rats (n = 6 at all ages). We used western blotting to detect heat shock proteins (HSPs) and cytoskeleton- or neurotransmission-related proteins in the developing astroglia. The GSM signal had no significant effect on the abundance of HSP60, HSC70 or HSP90, of serine racemase, glutamate transporters including GLT1 and GLAST, or of glial fibrillary acid protein (GFAP) in either total or soluble tissue extracts. Imunohistochemical detection of CD68 antigen in brain sections from pseudo-exposed and exposed animals did not reveal any differences in the morphology or distribution of microglial cells. These results provide no evidence for acute cell stress or glial reactions indicative of early neural cell damage, in developing brains exposed to 1,800 MHz signals in the range of SAR used in our study.

(E) Wiholm C, Lowden A, Kuster N, Hillert L, Arnetz BB, Akerstedt T, Moffat SD.Mobile phone exposure and spatial memory. Bioelectromagnetics. 30(1):59-65, 2009. (HU, BE)

Radiofrequency (RF) emission during mobile phone use has been suggested to impair cognitive functions, that is, working memory. This study investigated the effects of a 2 1/2 h RF exposure (884 MHz) on spatial memory and learning, using a double-blind repeated measures design. The exposure was designed to mimic that experienced during a real-life mobile phone conversation. The design maximized the exposure to the left hemisphere. The average exposure was peak spatial specific absorption rate (psSAR10g) of 1.4 W/kg. The primary outcome measure was a "virtual" spatial navigation task modeled after the commonly used and validated Morris Water Maze. The distance traveled on each trial and the amount of improvement across trials (i.e., learning) were used as dependent variables. The participants were daily mobile phone users, with and without symptoms attributed to regular mobile phone use. Results revealed a main effect of RF exposure and a significant RF exposure by group effect on distance traveled during the trials. The symptomatic group improved their performance during RF exposure while there was no such effect in the non-symptomatic group. Until this new finding is further investigated, we can only speculate about the cause.

(E) Xiong L, Sun CF, Zhang J, Gao YB, Wang LF, Zuo HY, Wang SM, Zhou HM, Xu XP, Dong J, Yao BW, Zhao L, Peng RY. Microwave Exposure Impairs Synaptic Plasticity in the Rat Hippocampus and PC12 Cells through Over-activation of the NMDA Receptor Signaling Pathway. Biomed Environ Sci. 28(1):13-24, 2015. (AS, CE, ME, CH)

OBJECTIVE: The aim of this study is to investigate whether microwave exposure would affect the N-methyl-D-aspartate receptor (NMDAR) signaling pathway to establish whether this plays a role in synaptic plasticity impairment. METHODS: 48 male Wistar rats were exposed to 30 mW/cm2 microwave for 10 min every other day for three times. Hippocampal structure was observed through H&E staining and transmission electron microscope. PC12 cells were exposed to 30 mW/cm2 microwave for 5 min and the synapse morphology was visualized with scanning electron microscope and atomic force microscope. The release of amino acid neurotransmitters and calcium influx were detected. The expressions of several key NMDAR signaling molecules were evaluated. RESULTS: Microwave exposure caused injury in rat hippocampal structure and PC12 cells, especially the structure and quantity of synapses. The ratio of glutamic acid and gamma-aminobutyric acid neurotransmitters was increased and the intracellular calcium level was elevated in PC12 cells. A significant change in NMDAR subunits (NR1, NR2A, and NR2B) and related signaling molecules (Ca2+/calmodulin-dependent kinase II gamma and phosphorylated cAMP-response element binding protein) were examined. CONCLUSION: 30 mW/cm2 microwave exposure resulted in alterations of synaptic structure, amino acid neurotransmitter release and calcium influx. NMDAR signaling molecules were closely associated with impaired synaptic plasticity.

(E) Xu F, Bai Q, Zhou K, Ma L, Duan J, Zhuang F, Xie C, Li W, Zou P, Zhu C. Age-dependent acute interference with stem and progenitor cell proliferation in the hippocampus after exposure to 1800 MHz electromagnetic radiation. Electromagn Biol Med. 36(2):158-166, 2017. (AS, CE, CC, AD)

To investigate the effects of exposure to an 1800 MHz electromagnetic field on cell death and cell proliferation in the developing brain, postnatal day 7 (P7) and P21 healthy Kunming mice were randomly assigned into the experimental and control groups. The experimental groups were exposed to an 1800 MHz electromagnetic field for 8 h daily for three consecutive days. The thymidine analog 5-bromo-2-deoxyuridine (BrdU) was injected intraperitoneally 1 h before each exposure session, and all animals were sacrificed 24 h after the last exposure. Cell death and proliferation markers were detected by immunohistochemistry in the dentate gyrus of the hippocampus. Electromagnetic exposure has no influence on cell death in the dentate gyrus of the hippocampus in P7 and P21 mice as indicated by active caspase-3 immunostaining and Fluoro-Jade labeling. The basal cell proliferation in the hippocampus was higher in P7 than in P21 mice as indicated by the number of cells labeled with BrdU and by immunohistochemical staining for phosphor-histone H3 (PHH3) and brain lipid-binding protein (BLBP). Electromagnetic exposure stimulated DNA synthesis in P7 neural stem and progenitor cells, but reduced cell division and the total number of stem cells in the hippocampus as indicated by increased BrdU labeling and reduced PHH3 and BLBP labeling compared to P7 control mice. There were no significant changes in cell proliferation in P21 mice after exposure to the electromagnetic field. These results indicate that interference with stem cell proliferation upon short-term exposure to an 1800 MHz electromagnetic field depends on the developmental stage of the brain.

(E) Xu S, Zhou Z, Zhang L, Yu Z, Zhang W, Wang Y, Wang X, Li M, Chen Y, Chen C, He M, Zhang G, Zhong M. Exposure to 1800 MHz radiofrequency radiation induces oxidative damage to mitochondrial DNA in primary cultured neurons. Brain Res. 1311:189-196, 2010. (CS, CH, OX)

Increasing evidence indicates that oxidative stress may be involved in the adverse effects of radiofrequency (RF) radiation on the brain. Because mitochondrial DNA (mtDNA) defects are closely associated with various nervous system diseases and mtDNA is particularly susceptible to oxidative stress, the purpose of this study was to determine whether radiofrequency radiation can cause oxidative damage to mtDNA. In this study, we exposed primary cultured cortical neurons to pulsed RF electromagnetic fields at a frequency of 1800 MHz modulated by 217 Hz at an average special absorption rate (SAR) of 2 W/kg. At 24 h after exposure, we found that RF radiation induced a significant increase in the levels of 8-hydroxyguanine (8-OHdG), a common biomarker of DNA oxidative damage, in the mitochondria of neurons. Concomitant with this finding, the copy number of mtDNA and the levels of mitochondrial RNA (mtRNA) transcripts showed an obvious reduction after RF exposure. Each of these mtDNA disturbances could be reversed by pretreatment with melatonin, which is known to be an efficient antioxidant in the brain. Together, these results suggested that 1800 MHz RF radiation could cause oxidative damage to mtDNA in primary cultured neurons. Oxidative damage to mtDNA may account for the neurotoxicity of RF radiation in the brain.

(E) Yan JG, Agresti M, Zhang LL, Yan Y, Matloub HS. Upregulation of specific mRNA levels in rat brain after cell phone exposure. Electromagn Biol Med. 27(2):147-154, 2008. (AS, CE, CH)

Adult Sprague-Dawley rats were exposed to regular cell phones for 6 h per day for 126 days (18 weeks). RT-PCR was used to investigate the changes in levels of mRNA synthesis of several injury-associated proteins. Calcium ATPase, Neural Cell Adhesion Molecule, Neural Growth Factor, and Vascular Endothelial Growth Factor were evaluated. The results showed statistically significant mRNA up-regulation of these proteins in the brains of rats exposed to cell phone radiation. These results indicate that relative chronic exposure to cell phone microwave radiation may result in cumulative injuries that could eventually lead to clinically significant neurological damage.

(E) Yang L, Chen Q, Lv B, Wu T. Long-Term Evolution Electromagnetic Fields Exposure Modulates the Resting State EEG on Alpha and Beta Bands. Clin EEG Neurosci. 48:168-175, 2017. (HU, EE)

Long-term evolution (LTE) wireless telecommunication systems are widely used globally, which has raised a concern that exposure to electromagnetic fields (EMF) emitted from LTE devices can change human neural function. To date, few studies have been conducted on the effect of exposure to LTE EMF. Here, we evaluated the changes in electroencephalogram (EEG) due to LTE EMF exposure. An LTE EMF exposure system with a stable power emission, which was equivalent to the maximum emission from an LTE mobile phone, was used to radiate the subjects. Numerical simulations were conducted to ensure that the specific absorption rate in

the subject's head was below the safety limits. Exposure to LTE EMF reduced the spectral power and the interhemispheric coherence in the alpha and beta bands of the frontal and temporal brain regions. No significant change was observed in the spectral power and the inter-hemispheric coherence in different timeslots during and after the exposure. These findings also corroborated those of our previous study using functional magnetic resonant imaging.

(E) Yang XS, He GL, Hao YT, Xiao Y, Chen CH, Zhang GB, Yu ZP. Exposure to 2.45 GHz electromagnetic fields elicits an HSP-related stress response in rat hippocampus. Brain Res Bull. 88(4):371-378, 2012. (AS, CH)

The issue of possible neurobiological effects of the electromagnetic field (EMF) exposure is highly controversial. To determine whether electromagnetic field exposure could act as an environmental stimulus capable of producing stress responses, we employed the hippocampus, a sensitive target of electromagnetic radiation, to assess the changes in its stress-related gene and protein expression after EMF exposure. Adult male Sprague-Dawley rats with body restrained were exposed to a 2.45 GHz EMF at a specific absorption rate (SAR) of 6 W/kg or sham conditions. cDNA microarray was performed to examine the changes of gene expression involved in the biological effects of electromagnetic radiation. Of 2048 candidate genes, 23 upregulated and 18 downregulated genes were identified. Of these differential expression genes, two heat shock proteins (HSP), HSP27 and HSP70, are notable because expression levels of both proteins are increased in the rat hippocampus. Result from immunocytochemistry revealed that EMF caused intensive staining for HSP27 and HSP70 in the hippocampus, especially in the pyramidal neurons of cornu ammonis 3 (CA3) and granular cells of dentate gyrus (DG). The gene and protein expression profiles of HSP27 and HSP70 were further confirmed by reverse transcription polymerase chain reaction (RT-PCR) and Western blot. Our data provide direct evidence that exposure to electromagnetic fields elicits a stress response in the rat hippocampus.

(E) Yang X, He G, Hao Y, Chen C, Li M, Wang Y, Zhang G, Yu Z. The role of the JAK2-STAT3 pathway in pro-inflammatory responses of EMF-stimulated N9 microglial cells. J Neuroinflammation. 7:54, 2010. (CS, CH)

BACKGROUND: In several neuropathological conditions, microglia can become overactivated and cause neurotoxicity by initiating neuronal damage in response to pro-inflammatory stimuli. Our previous studies have shown that exposure to electromagnetic fields (EMF) activates cultured microglia to produce tumor necrosis factor (TNF)-α and nitric oxide (NO) through signal transduction involving the activator of transcription STAT3. Here, we investigated the role of STAT3 signaling in EMF-induced microglial activation and pro-inflammatory responses in more detail than the previous study. **METHODS:** N9 microglial cells were treated with EMF exposure or a sham treatment, with or without pretreatment with an inhibitor (Pyridone 6, P6) of the Janus family of tyrosine kinases (JAK). The activation state of microglia was assessed via immunoreaction using the microglial marker CD11b. Levels of inducible nitric oxide synthase (iNOS), TNF-α and NO were measured using real-time reverse transcription-polymerase chain reaction (RT-PCR), enzyme-linked immunosorbent assay (ELISA) and the nitrate reductase

method. Activation of JAKs and STAT3 proteins was evaluated by western blotting for specific tyrosine phosphorylation. The ability of STAT3 to bind to DNA was detected with an electrophoresis mobility shift assay (EMSA). **RESULTS:** EMF was found to significantly induce phosphorylation of JAK2 and STAT3, and DNA-binding ability of STAT3 in N9 microglia. In addition, EMF dramatically increased the expression of CD11b, TNF-α and iNOS, and the production of NO. P6 strongly suppressed the phosphorylation of JAK2 and STAT3 and diminished STAT3 activity in EMF-stimulated microglia. Interestingly, expression of CD11b as well as gene expression and production of TNF-α and iNOS were suppressed by P6 at 12 h, but not at 3 h, after EMF exposure. **CONCLUSIONS:** EMF exposure directly triggers initial activation of microglia and produces a significant pro-inflammatory response. Our findings confirm that the JAK2-STAT3 pathway may not mediate this initial microglial activation but does promote pro-inflammatory responses in EMF-stimulated microglial cells. Thus, the JAK2-STAT3 pathway might be a therapeutic target for reducing pro-inflammatory responses in EMF-activated microglia.

(NE) Yilmaz F, Dasdag S, Akdag MZ, Kilinc N. Whole-body exposure of radiation emitted from 900 MHz mobile phones does not seem to affect the levels of anti-apoptotic bcl-2 protein. Electromagn Biol Med. 27(1):65-72, 2008. (AS, CH)

The purpose of the present study was to investigate the anti-apoptotic bcl-2 protein in rat brain and testes after whole-body exposure to radiation emitted from 900 MHz cellular phones. Two groups (sham and experimental) of Sprague-Dawley rats of eight rats each were used in the study. Exposure began approximately 10 min after transferring into the exposure cages, a period of time when rats settled down to a prone position and selected a fixed location inside the cage spontaneously. For the experimental group, the phones were in the speech condition for 20 min per day for 1 month. The same procedure was applied to the sham group rats, but the phones were turned off. Immunohistochemical staining of bcl-2 was performed according to the standardized avidin-biotin complex method. The results of this study showed that 20 min of the radiation emitted from 900 MHz cellular phones did not alter anti-apoptotic bcl-2 protein in the brain and testes of rats. We speculate that bcl-2 may not be involved in the effects of radiation on the brain and testes of rats.

(E) Yilmaz A, Yilmaz N, Serarslan Y, Aras M, Altas M, Ozgür T, Sefil F. The effects of mobile phones on apoptosis in cerebral tissue: an experimental study on rats. Eur Rev Med Pharmacol Sci. 18(7):992-1000, 2014. (AS, CE, CH)

INTRODUCTION: The concern about mobile phone effects is increasing as the number of users increasing too. Different studies have different results, so this topic is still open to discussion. Aim of this report was to investigate the effects of the mobile phones on the Bcl-2 gene and p53 proteins in rat brains. **MATERIALS AND METHODS:** In the study group of 10 rats; mobile phones that spread EMW at a frequency between 1900-2100 MHz and Specific Absorption Rate range between 0.005 W/kg and 0.288 W/kg (Dialing mode), 0.004 W/kg and 0.029 W/kg (Calling mode) were attached to rat ears for simulating usage in daily life for 7 times a day during 5 minutes (3 seconds dialing mode, 4 minutes and 47 seconds of calling mode) for a four

week period. Sham group (n=10) rats were only immobilized without EMW exposure. Another group of rats (n=10) were counted as control without any application. immunohistopathological examination was performed for p53 and Bcl-2 expression. **RESULTS:** Immunohistopathological examinations revealed that the samples in the study group had more p53 and Bcl-2 positive stained cells and they were stained denser. In both evaluations, these differences between the study and control group were found statistically significant ($p < 0.003$); In Bcl-2 evaluation statistically significant difference was found between study and sham group to ($p < 0.005$); however, the p53 evaluation between the study and the sham group did not show any statistically significant difference ($p > 0.005$). **CONCLUSIONS:** Our results showed that the electro-magnetic waves emitted by the mobile phones may have effect on apoptosis. Besides, obtained data revealed that more realistic application of mobile phones during experiments is more important as expected.

(E) Yogesh S, Abha S, Priyanka S. Mobile usage and sleep patterns among medical students. Indian J Physiol Pharmacol. 58(1):100-103, 2014. (HU, CE, BE, SL)

Exposure of humans to radio frequency electromagnetic field (EMF) both during receiving and transmitting the signals has amplified public and scientific debate about possible adverse effects on human health. The study was designed with the objective of assessing the extent of mobile phone use amongst medical students and finding correlation if any between the hours of usage of mobile to sleep pattern and quality. hundred medical students grouped as cases (n = 57) (> 2 hours/day of mobile usage) and control (n = 43) (≤ 2 hours/day of mobile usage) were examined for their sleep quality & pattern by Pittsburg sleep Quality Index (PSQI). Differences between groups were examined with the Mann Whitney "U" test for proportions (Quantitative values) and with Student's t test for continuous variables. The association of variables was analyzed by Spearman Rank's correlation. Probability was set at < 0.05 as significant. Sleep disturbance, latency and day dysfunction was more in cases especially females. A significant association of hours of usage and sleep indices were observed in both genders (males r = 0.25; p = 0.04, females r = 0.31; p = 0.009). Evening usage of mobile phone in cases showed a statistically significant negative association (-0.606; p = 0.042) with Sleep quality (higher PSQI means sleep deprivation). Students using mobile for > 2 hours/day may cause sleep deprivation and day sleepiness affecting cognitive and learning abilities of medical students.

***(E) Yuan K, Qin W, Wang G, Zeng F, Zhao L, Yang X, Liu P, Liu J, Sun J, von Deneen KM, Gong Q, Liu Y, Tian J. Microstructure abnormalities in adolescents with internet addiction disorder. PLoS One. 6(6):e20708, 2011. (HU, ME) (*Effects observed probably not caused by exposure to RFR.)**

BACKGROUND: Recent studies suggest that internet addiction disorder (IAD) is associated with structural abnormalities in brain gray matter. However, few studies have investigated theeffects of internet addiction on the microstructural integrity of major neuronal fiber pathways, and almost no studies have assessed the microstructural changes with the duration of internet addiction. **METHODOLOGY/PRINCIPAL FINDINGS:** We investigated the morphology of the brain in adolescents with IAD (N = 18) using an optimized voxel-based morphometry

(VBM) technique, and studied the white matter fractional anisotropy (FA) changes using the diffusion tensor imaging (DTI) method, linking these brain structural measures to the duration of IAD. We provided evidences demonstrating the multiple structural changes of the brain in IAD subjects. VBM results indicated the decreased gray matter volume in the bilateral dorsolateral prefrontal cortex (DLPFC), the supplementary motor area (SMA), the orbitofrontal cortex (OFC), the cerebellum and the left rostral ACC (rACC). DTI analysis revealed the enhanced FA value of the left posterior limb of the internal capsule (PLIC) and reduced FA value in the white matter within the right parahippocampal gyrus (PHG). Gray matter volumes of the DLPFC, rACC, SMA, and white matter FA changes of the PLIC were significantly correlated with the duration of internet addiction in the adolescents with IAD. **CONCLUSIONS:** Our results suggested that long-term internet addiction would result in brain structural alterations, which probably contributed to chronic dysfunction in subjects with IAD. The current study may shed further light on the potential brain effects of IAD.

(E) Zareen N, Khan MY, Ali Minhas L. Derangement of chick embryo retinal differentiation caused by radiofrequency electromagnetic fields. Congenit Anom (Kyoto). 49(1):15-19, 2009. (AS, CE, ME, DE)

The possible adverse effects of radiofrequency electromagnetic fields (EMF) emitted from mobile phones present a major public concern. Biological electrical activities of the human body are vulnerable to interference from oscillatory aspects of EMF, which affect fundamental cellular activities, in particular, the highly active development process of embryos. Some studies highlight the possible health hazards of EMF, while others contest the hypothesis of biological impact of EMF. The present study was designed to observe the histomorphological effects of EMF emitted by a mobile phone on the retinae of developing chicken embryos. Fertilized chicken eggs were exposed to a ringing mobile set on silent tone placed in the incubator at different ages of development. After exposure for the scheduled duration the retinae of the embryos were dissected out and processed for histological examination. The control and experimental embryos were statistically compared for retinal thickness and epithelial pigmentation grades. Contrasting effects of EMF on the retinal histomorphology were noticed, depending on the duration of exposure. The embryos exposed for 10 post-incubation days exhibited decreased retinal growth and mild pigmentation of the epithelium. Growth retardation reallocated to growth enhancement on increasing EMF exposure for 15 post-incubation days, with a shift of pigmentation grade from mild to intense. We conclude that EMF emitted by a mobile phone cause derangement of chicken embryo retinal differentiation.

(E) Zhang JP, Zhang KY, Guo L, Chen QL, Gao P, Wang T, Li J, Guo GZ, Ding GR. Effects of 1.8 GHz Radiofrequency Fields on the Emotional Behavior and Spatial Memory of Adolescent Mice. Int J Environ Res Public Health. 2017 Nov 5;14(11). pii: E1344. doi: 10.3390/ijerph14111344. (AS, CE, BE, CH)

The increasing use of mobile phones by teenagers has raised concern about the cognitive effects of radiofrequency (RF) fields. In this study, we investigated the effects of 4-week

exposure to a 1.8 GHz RF field on the emotional behavior and spatial memory of adolescent male mice. Anxiety-like behavior was evaluated by open field test (OFT) and elevated plus maze (EPM) test, while depression-like behavior was evaluated by sucrose preference test (SPT), tail suspension test (TST) and forced swim test (FST). The spatial learning and memory ability were evaluated by Morris water maze (MWM) experiments. The levels of amino acid neurotransmitters were determined by liquid chromatography-mass spectrometry (LC-MS). The histology of the brain was examined by hematoxylin-eosin (HE) staining. It was found that the depression-like behavior, spatial memory ability and histology of the brain did not change obviously after RF exposure. However, the anxiety-like behavior increased in mice, while, the levels of γ-aminobutyric acid (GABA) and aspartic acid (Asp) in cortex and hippocampus significantly decreased after RF exposure. These data suggested that RF exposure under these conditions do not affect the depression-like behavior, spatial memory and brain histology in adolescent male mice, but it may however increase the level of anxiety, and GABA and Asp were probably involved in this effect.

(E) Zhang SZ, Yao GD, Lu DQ, Chiang H, Xu ZP. [Effect of 1.8 GHz radiofrequency electromagnetic fields on gene expression of rat neurons]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 26(8):449-452, 2008. [Article in Chinese] (CS, CH, WS)

OBJECTIVE: To investigate the changes of gene expression in rat neuron induced by 1.8 GHz radiofrequency electromagnetic fields (RF EMF) to screen for RF EMF-responsive genes and the effect of different exposure times and modes on the gene expression in neuron. METHODS: Total RNA was extracted immediately and purified from the primary culture of neurons after intermittent exposed or sham-exposed to a frequency of 1.8 GHz RF EMF for 24 hours at an average special absorption rate (SAR) of 2 W/kg. Affymetrix Rat Neurobiology U34 array was applied to investigate the changes of gene expression in rat neuron. Differentially expressed genes (Egr-1, Mbp and Plp) were further confirmed by semi-quantitative revere transcription polymerase chain reaction (RT PCR). The expression levels of Egr-1, Mbp and Plp were observed at different exposure times (6, 24 h) and modes (intermittent and continuous exposure). RESULTS: Among 1200 candidate genes, 24 up-regulated and 10 down-regulated genes were found by using Affymetrix microarray suite software 5.0 which are associated with multiple cellular functions (cytoskeleton, signal transduction pathway, metabolism, etc.) after functional classification. Under 24 h and 6 h intermittent exposure, Egr-1 and Plp in experiment groups showed statistic significance ($P < 0.05$) compared with the control groups, while expression of Mbp did not change significantly ($P > 0.05$). After 24 h continuous exposure, Egr-1 and Mbp in experiment groups showed statistic significance ($P < 0.05$) compared with the control group, while expression of Plp did not change significantly ($P > 0.05$). Under the same exposure mode 6 h, expression of all the 3 genes did not change significantly. Different times (6, 24 h) and modes (intermittent and continuous exposure) of exposure exerted remarkable different influences on the expression of Egr-1, Mbp, Plp genes ($P < 0.01$). CONCLUSION: The changes of many genes transcription were involved in the effect of 1.8 GHz RF EMF on rat neurons; Down-regulation of Egr-1 and up-regulation of Mbp, Plp indicated the negative effects of RF EMF on neurons; The effect of RF intermittent exposure on gene expression was more obvious than

that of continuous exposure; The effect of 24 h RF exposure (both intermittent and continuous) on gene expression was more obvious than that of 6 h (both intermittent and continuous).

(E) Zhang Y, She F, Li L, Chen C, Xu S, Luo X, Li M, He M, Yu Z. p25/CDK5 is partially involved in neuronal injury induced by radiofrequency electromagnetic field exposure. Int J Radiat Biol. 2013 Jul 29. [Epub ahead of print] (CS, CC)

Purpose: Several studies suggest that radiofrequency electromagnetic field (RF-EMF) exposure can induce neuronal injury. The aim of the present work was to investigate whether the cyclin-dependent kinase 5 (CDK5) pathway is involved in neuronal injury induced by RF-EMF exposure. Materials and methods: Newborn Sprague-Dawley rats' primary cultured cortical neurons were exposed to pulsed 2.45 GHz RF-EMF for 10 min. The cellular viability was assessed using the 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay. The apoptosis was assessed by Hoechst 33342 and terminal deoxynucleotidyl transferase (TdT)-mediated dUTP nick-end labeling co-staining. The protein expressions of CDK5, p35, p25, and phosphorylated tau at Ser^{404} were examined by Western blot analysis. The CDK5 activity was detected using a histone-H1 kinase assay. Results: The cellular viability of neurons was significantly decreased ($p < 0.01$, Partial Eta Squared [η_p^2]: 0.554), and the percentage of apoptotic nuclei ($p < 0.01$, $\eta_p^2 = 0.689$), activity of CDK5 ($p < 0.05$, $\eta_p^2 = 0.589$), ratio of p25 and p35 ($p < 0.05$, $\eta_p^2 = 0.670$), levels of tau phosphorylation at Ser^{404} ($p < 0.01$, $\eta_p^2 = 0.896$) were significantly increased after RF-EMF exposure. No significant change was detected in CDK5 expression after RF-EMF exposure. Pretreatment with Roscovitine (a CDK5 inhibitor) significantly blocked the RF-EMF-induced decrease of cellular viability ($p < 0.05$, $\eta_p^2 = 0.398$) and tau hyperphosphorylation at Ser^{404} ($p < 0.01$, $\eta_p^2 = 0.917$), but did not significantly block the RF-EMF-induced apoptosis ($p > 0.05$, $\eta_p^2 = 0.130$). Conclusions: These results suggest that abnormal activity of p25/CDK5 is partially involved in primary cultured cortical neuron injury induced by RF-EMF exposure.

(E) Zhang Y, Li Z, Gao Y, Zhang C. Effects of fetal microwave radiation exposure on offspring behavior in mice. J Radiat Res. 56:261-268, 2015. (AS, CE, BE, DE)

The recent rapid development of electronic communication techniques is resulting in a marked increase in exposure of humans to electromagnetic fields (EMFs). This has raised public concerns about the health hazards of long-term environmental EMF exposure for fetuses and children. Some studies have suggested EMF exposure in children could induce nervous system disorders. However, gender-dependent effects of microwave radiation exposure on cognitive dysfunction have not previously been reported. Here we investigated whether in utero exposure to 9.417-GHz microwave throughout gestation (Days 3.5-18) affected behavior, using the open field test (OFT), elevated-plus maze (EPM), tail suspension test (TST), forced swimming test (FST) and Morris water maze (MWM). We found that mice showed less movement in the center of an open field (using the OFT) and in an open arm (using the EPM) after in utero exposure to 9.417-GHz radiation, which suggested that the mice had increased anxiety-related behavior. Mice demonstrated reduced immobility in TST and FST after in utero exposure to 9.417-GHz radiation, which suggested that the mice had decreased depression-related

behavior. From the MWM test, we observed that male offspring demonstrated decreased learning and memory, while females were not affected in learning and memory, which suggested that microwaves had gender-dependent effects. In summary, we have provided the first experimental evidence of microwaves inducing gender-dependent effects.

(E) Zhao R, Zhang S, Xu Z, Ju L, Lu D, Yao G. Studying gene expression profile of rat neuron exposed to 1800MHz radiofrequency electromagnetic fields with cDNA microassay. Toxicology. 235(3):167-175, 2007. (CS, CH)

A widespread use of mobile phone (MP) evokes a growing concern for their possible adverse effects on human, especially the brain. Gene expression is a unique way of characterizing how cells and organism adapt to changes in the external environment, so the aim of this investigation was to determine whether 1800 MHz radiofrequency electromagnetic fields (RF EMF) can influence the gene expression of neuron. Affymetrix Rat Neurobiology U34 array was applied to investigate the changes of gene expression in rat neuron after exposed to the pulsed RF EMF at a frequency of 1800 MHz modulated by 217 Hz which is commonly used in MP. Among 1200 candidate genes, 24 up-regulated genes and 10 down-regulated genes were identified after 24-h intermittent exposure at an average special absorption rate (SAR) of 2 W/kg, which are associated with multiple cellular functions (cytoskeleton, signal transduction pathway, metabolism, etc.) after functional classification. The results were further confirmed by quantitative real-time polymerase chain reaction (RT PCR). The present results indicated that the gene expression of rat neuron could be altered by exposure to RF EMF under our experimental conditions.

(E) Zhao TY, Zou SP, Knapp PE. Exposure to cell phone radiation up-regulates apoptosis genes in primary cultures of neurons and astrocytes. Neurosci Lett. 412(1):34-38, 2007. (CS, CH)

The health effects of cell phone radiation exposure are a growing public concern. This study investigated whether expression of genes related to cell death pathways are dysregulated in primary cultured neurons and astrocytes by exposure to a working Global System for Mobile Communication (GSM) cell phone rated at a frequency of 1900MHz. Primary cultures were exposed to cell phone emissions for 2h. We used array analysis and real-time RT-PCR to show up-regulation of caspase-2, caspase-6 and Asc (apoptosis associated speck-like protein containing a card) gene expression in neurons and astrocytes. Up-regulation occurred in both "on" and "stand-by" modes in neurons, but only in "on" mode in astrocytes. Additionally, astrocytes showed up-regulation of the Bax gene. The effects are specific since up-regulation was not seen for other genes associated with apoptosis, such as caspase-9 in either neurons or astrocytes, or Bax in neurons. The results show that even relatively short-term exposure to cell phone radiofrequency emissions can up-regulate elements of apoptotic pathways in cells derived from the brain, and that neurons appear to be more sensitive to this effect than astrocytes.

(E) Zheng F, Gao P, He M, Li M, Wang C, Zeng Q, Zhou Z, Yu Z, Zhang L. Association between mobile phone use and inattention in 7102 Chinese adolescents: a population-based cross-sectional study. BMC Public Health. 2014 Oct 1;14(1):1022. [Epub ahead of print] (HU, CE, BE)

BACKGROUND: The dramatic growth of mobile phone (MP) use among young people has increased interest in its possible health hazards in this age group. The aim of this cross-sectional study was to investigate the association between MP use and inattention in adolescents. METHODS: A total of 7720 middle school students were involved in this cross-sectional study. Inattention was assessed as defined for the Attention Deficit component of Attention deficit/Hyperactivity disorder (ADHD) by the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev. [DSM-IV-TR]). The demographic characteristics and information on MP use were included in the questionnaire. Chi-square tests and logistic regression models were used to analyze the data. RESULTS: In total, 7102 (91.99%) valid questionnaires were obtained. After adjusted for confounders, inattention in adolescents was significantly associated with MP ownership, the time spent on entertainment on MP per day, the position of the MP during the day and the mode of the MP at night. The strongest association between inattention and the time spent on the MP was among students who spent more than 60 minutes per day playing on their MP. CONCLUSIONS: Our study shows some associations between MP use and inattention in Chinese adolescents. Decreasing MP usage to less than 60 minutes per day may help adolescents to stay focused and centered.

(E) Zuo H, Lin T, Wang D, Peng R, Wang S, Gao Y, Xu X, Zhao L, Wang S, Su Z. RKIP regulates neural cell apoptosis induced by exposure to microwave radiation partly through the MEK/ERK/CREB pathway. Mol Neurobiol. 2014 Aug 10. [Epub ahead of print] (CS, CC)

In the present study, we investigated whether Raf-1 kinase inhibitory protein (RKIP) is important for neural cell apoptosis induced by microwave exposure and explored the role of MEK/ERK/CREB pathway regulated by RKIP in the apoptosis. Differentiated PC12 cells were exposed to continuous microwave radiation at 2.856 GHz for 5 min with average power density of 30 mW/cm2. RKIP sense and anti-sense recombinant plasmids were constructed and transfected into PC12 cells, respectively. Terminal deoxynucleotidyl transferase (TdT)-mediated dUTP nick end labeling (TUNEL) staining and caspase-3 activity assay were used to detect cell apoptosis. The results showed that RKIP was downregulated after microwave exposure while the MEK/ERK/CREB signaling pathway was activated excessively. Moreover, the ratio of Bcl-2/Bax decreased, activity of caspase-3 increased, and thus apoptotic DNA fragmentation increased. RKIP overexpression significantly inhibited the phosphorylation of MEK, ERK, and CREB, while RKIP downregulation had the reverse effect. Furthermore, U0126 was found to antagonize the changes caused by RKIP downregulation after exposure to radiation. In conclusion, RKIP plays an important role in the neural cell apoptosis induced by microwave radiation, and the regulation of cell apoptosis by RKIP is partly through the MEK/ERK/CREB pathway. This suggests that RKIP may act as a key regulator of neuronal damage caused by

microwave radiation. Extremely Low-Frequency Electromagnetic Fields Cause G1 Phase Arrest through the Activation of the ATM-Chk2-p21 Pathway