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#### Over 380 Studies Showing Neurological Effects From Radio Frequency Radiation

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#### **Neurological Effects**

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. Abstract. 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 entorhinalparahippocampal regions which participate in the ORT memory task.

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. 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.

### Hocking B, Westerman R, Neurological abnormalities associated with Mobile phone use. Occup Med 50: 366-368, 2000.

Dysaesthesiae of the scalp after mobile phone use have been previously reported but the pathological basis of these symptoms has been unclear. <u>We report finding a</u> <u>neurological abnormality in a patient after prolonged use of a mobile phone. He had</u> <u>permanent unilateral dysaesthesiae of the scalp, slight loss of sensation, and</u> <u>abnormalities on current perception threshold testing of cervical and trigeminal nerves.</u> A neurologist found no other disease. The implications regarding health effects of mobile phones and radio-frequency radiation is discussed.

#### 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, 2013. 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.

## Maier R, Greter SE, Maier N. Effects of pulsed electromagnetic fields on cognitive processes - a pilot study on pulsed field interference with cognitive regeneration. Acta Neurol Scand. 110(1):46-52, 2004.

BACKGROUND: Due to the ubiquitous use of cellular phones much has been speculated

on secondary effects of electromagnetic irradiation emitted by those. Additionally, several studies have reported vegetative alterations as well as effects on the neuronal and molecular levels in humans. Here, using a psycho-physiological test paradigm, we examined effects of exposure to pulsed electromagnetic fields on cognitive performance. MATERIALS AND METHODS: In 11 volunteers, we tested cognitive processing under field exposure (GSM standard) and under field-free conditions. To examine the hypothesized effect of pulsed fields, we applied an auditory discrimination task and determined the participant's current 'Order Threshold' value. Following a first test cycle, the volunteers had to relax for 50 min while being, or not, exposed to pulsed electromagnetic fields. Subsequently, the test was repeated. Data acquired before and after the resting phase were compared from both experimental conditions. RESULTS: We found that nine of the 11 test participants (81.8%) showed worse results in their auditory discrimination performance upon field exposure as compared with control conditions. Group data comparison revealed a statistical significance of P = 0.0105. CONCLUSION: We could show that the participants' cognitive performance was impaired after exposure to pulsed electromagnetic fields. With regard to this finding, we recommend that the use of cellular phones should be restricted generally and in particular in respect of physical hazard of high-risk groups, e.g. elderly, children and ill people.

## Maier R, Greter SE, Maier N. Effects of pulsed electromagnetic fields on cognitive processes - a pilot study on pulsed field interference with cognitive regeneration. Acta Neurol Scand. 110(1):46-52, 2004.

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### Hocking B, Westerman R. Neurological effects of radiofrequency radiation. Occup Med (Lond) 53(2):123-127, 2003.

BACKGROUND: The health effects of radiofrequency radiation (RFR) and the adequacy of the safety standards are a subject of debate. One source of human data is case reports regarding peripheral neurological effects of RFR, mainly noxious sensations or dysaesthesiae. Aim To investigate health effects, neurophysiological mechanisms and safety levels for RFR. METHODS: We conducted a literature search for case reports and case series associated with mobile phone technology as well as other RFR sources using specific search terms on PubMed. RESULTS: We identified 11 original articles detailing case reports or case series and matching the search criteria. Five of the identified papers were written by at least one of the authors (B.H. or R.W.). CONCLUSIONS: Cases have arisen after exposure to much of the radiofrequency range. In some cases, symptoms are transitory but lasting in others. After very high exposures, nerves may be grossly injured. After lower exposures, which may result in dysaesthesia, ordinary nerve conduction studies find no abnormality but current perception threshold studies have found abnormalities. Only a small proportion of similarly exposed people develop symptoms. The role of modulations needs clarification. Some of these observations are not consistent with the prevailing hypothesis that all health effects of RFR arise from thermal mechanisms.

#### <u>Nittby H, Grafström G, Tian DP, Malmgren L, Brun A</u>, <u>Persson BR</u>, <u>Salford LG</u>, <u>Eberhardt</u> <u>J</u>. Cognitive impairment in rats after long-term exposure to GSM-900 mobile phone radiation. <u>Bioelectromagnetics.</u> 29:219-232, 2008.

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).

### Croft R, Chandler J, Burgess A, Barry R, Williams J, Clarke A. Acute mobile phone operation affects neural function in humans. Clin Neurophysiol 113(10):1623, 2002.

OBJECTIVES: Mobile phones (MP) are used extensively and yet little is known about the effects they may have on human physiology. There have been conflicting reports regarding the relation between MP use and the electroencephalogram (EEG). The

present study suggests that this conflict may be due to methodological differences such as exposure durations, and tests whether exposure to an active MP affects EEG as a function of time.METHODS: Twenty-four subjects participated in a single-blind fully counterbalanced cross-over design, where both resting EEG and phase-locked neural responses to auditory stimuli were measured while a MP was either operating or turned off.RESULTS: MP exposure altered resting EEG, decreasing 1-4Hz activity (right hemisphere sites), and increasing 8-12Hz activity as a function of exposure duration (midline posterior sites). MP exposure also altered early phase-locked neural responses, attenuating the normal response decrement over time in the 4-8Hz band, decreasing the response in the 1230Hz band globally and as a function of time, and increasing midline frontal and lateral posterior responses in the 30-45Hz band.<u>CONCLUSIONS:</u> <u>Active MPs affect neural function in humans and do so as a function of exposure</u> <u>duration</u>. The temporal nature of this effect may contribute to the lack of consistent results reported in the literature.

## <u>Eliyahu I, Luria R</u>, <u>Hareuveny R</u>, <u>Margaliot M</u>, <u>Meiran N</u>, <u>Shani G</u>. Effects of radiofrequency radiation emitted by cellular telephones on the cognitive functions of humans. <u>Bioelectromagnetics.</u>27(2):119-126, 2006.

The present study examined the effects of exposure to Electromagnetic Radiation emitted by a standard GSM phone at 890 MHz on human cognitive functions. This study attempted to establish a connection between the exposure of a specific area of the brain and the cognitive functions associated with that area. A total of 36 healthy righthanded male subjects performed four distinct cognitive tasks: spatial item recognition, verbal item recognition, and two spatial compatibility tasks. Tasks were chosen according to the brain side they are assumed to activate. All subjects performed the tasks under three exposure conditions: right side, left side, and sham exposure. The phones were controlled by a base station simulator and operated at their full power. We have recorded the reaction times (RTs) and accuracy of the responses. The experiments consisted of two sections, of 1 h each, with a 5 min break in between. The tasks and the exposure regimes were counterbalanced. The results indicated that the exposure of the left side of the brain slows down the left-hand response time, in the second-later-part of the experiment. This effect was apparent in three of the four tasks, and was highly significant in only one of the tests. The exposure intensity and its duration exceeded the common exposure of cellular phone users.

#### Narayanan SN, Kumar RS, Potu BK, Nayak S, Mailankot M. Spatial memory

**performance of Wistar rats exposed to mobile phone.** <u>Clinics.</u> 64(3):231-234, 2009. 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. <u>CONCLUSION: Mobile phone</u> 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.

#### Schneider J, Stangassinger M. Nonthermal Effects of Lifelong High-Frequency Electromagnetic Field Exposure on Social Memory Performance in Rats. Behav Neurosci. 2014 Jul 7. [Epub ahead of print]

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.

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. 2014 Dec 24. pii: S0031-9384(14)00663-5. doi: 10.1016/j.physbeh.2014.12.039. [Epub ahead of print] 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<sup>2</sup> 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<sub>1A, 2A, 2C</sub> receptors were measured. <u>We demonstrated that chronic</u> <u>exposure to microwave (2.856GHz, with the average power density of 5, 10, 20 and 30mW/cm<sup>2</sup>) 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<sub>1A</sub>R and 5-HT<sub>2C</sub>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.</u>

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. 2013 Jan 15. [Epub ahead of print] 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 longterm 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.

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

We tested the working hypothesis that electromagnetic fields from mobile phones (EMFs) affect <u>interhemispheric synchronization of cerebral rhythms, an important</u> <u>physiological feature of information transfer into the brain.</u> 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.

# <u>Vecchio F, Babiloni C, Ferreri F, Buffo P, Cibelli G, Curcio G, Dijkman SV, Melgari JM, Giambattistelli F, Rossini PM</u>. Mobile phone emission modulates inter-hemispheric functional coupling of EEG alpha rhythms in elderly compared to young subjects. <u>Clin Neurophysiol</u>. 121(2):163-171, 2010.

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 (45min) in one condition and was turned off (45min) in the other condition. Spectral coherence evaluated the interhemispheric synchronization of EEG rhythms at the following bands: delta (about 2-4Hz), theta (about 4-6Hz), alpha 1 (about 6-8Hz), alpha 2 (about 8-10Hz), and alpha 3 (about 10-12Hz). 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 8-12Hz) 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.

### Hocking B, Westerman R. Neurological changes induced by a mobile phone. Occup Med (Lond) 52(7):413-415, 2002.

Dysaesthesiae of the scalp after mobile phone use have been previously reported, but the basis for this has not been clear. We report a case of a 34-year-old journalist who complained of symptoms associated with use of a mobile phone. She agreed to a provocation study with her phone. Current perception threshold testing before and after exposure showed marked changes in the C-fibre nerves of the affected area compared with the opposite side. The case is supportive of a neurological basis for some cases of dysaesthesiae associated with mobile phone use.

## <u>Curcio G</u>, <u>Ferrara M</u>, <u>Moroni F</u>, <u>D'Inzeo G</u>, <u>Bertini M</u>, <u>De Gennaro L</u>. Is the brain influenced by a phone call? An EEG study of resting wakefulness. Neurosci Res. 53(3):265-270, 2005.

We recorded the resting electroencephalogram of 20 healthy subjects in order to investigate the effect of electromagnetic field (EMF) exposure on EEG waking activity and its temporal development. The subjects were randomly assigned to two groups and exposed, in double-blind conditions, to a typical mobile phone signal (902.40MHz, modulated at 217Hz, with an average power of 0.25W) before or during the EEG recording session. The results show that, under real exposure as compared to baseline and sham conditions, EEG spectral power was influenced in some bins of the alpha band. This effect was greater when the EMF was on during the EEG recording session than before it. The present data lend further support to the idea that pulsed high-frequency electromagnetic fields can affect normal brain functioning, also if no conclusions can be drawn about the possible health effects.

#### Vecchio F, Tombini M, Buffo P, Assenza G, Pellegrino G, Benvenga A, Babiloni C,

### <u>Rossini PM</u>. Mobile phone emission increases inter-hemispheric functional coupling of electroencephalographic alpha rhythms in epileptic patients. <u>Int J</u> <u>Psychophysiol.</u>84(2):164-171, 2012.

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 (45min) in the "GSM" condition and was turned off (45min) 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 2-4Hz), theta (about 4-6Hz), alpha1 (about 6-8Hz), alpha2 (about 8-10Hz), and alpha3 (about 10-12Hz). 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 8-12Hz) in the GSM than "Sham" condition. <u>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.</u>

## Balikci K, Cem Ozcan I, Turgut-Balik D, Balik HH. A survey study on some neurological symptoms and sensations experienced by long term users of mobile phones. Pathol Biol (Paris). 53(1):30-34, 2005.

A survey study was conducted to investigate the possible effects of mobile phone on headache, dizziness, extreme irritation, shaking in the hands, speaking falteringly, forgetfulness, neuro-psychological discomfort, increase in the carelessness, decrease of the reflex and clicking sound in the ears. There is no effect on dizziness, shaking in hands, speaking falteringly and neuro-psychological discomfort, but some <u>statistical evidences are found that mobile phone may cause headache, extreme irritation, increase in the carelessness, forgetfulness, decrease of the reflex and clicking sound in the ears.</u>

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. 2013 Jun 20. doi: 10.1002/bem.21801. [Epub ahead of print] 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

<u>contribute to cover the existing gap between safety research and applied biomedical</u> <u>science targeting the potential biological effects of environmental RF EMFs.</u>

## <u>Luria R</u>, <u>Eliyahu I</u>, <u>Hareuveny R</u>, <u>Margaliot M</u>, <u>Meiran N</u>. Cognitive effects of radiation emitted by cellular phones: the influence of exposure side and time.<u>Bioelectromagnetics.</u> 30(3):198-204, 2009.

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 leftside exposure condition was significantly longer than those of the right-side and shamexposure 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.

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. 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.

## <u>Qin F, Yuan H</u>, <u>Nie J</u>, <u>Cao Y</u>, <u>Tong J</u>. [Effects of nano-selenium on cognition performance of mice exposed in 1800 MHz radiofrequency fields]. <u>Wei Sheng Yan Jiu.</u> 43(1):16-21, 2014. [Article in Chinese]

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 conctral group were 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.

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

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).

## 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.

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)-1 $\beta$  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.

#### 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.

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.

#### <u>Lovisolo GA</u>, <u>Giardino L</u>, <u>Calzaà L</u>. Effect of radiofrequency electromagnetic field exposure on in vitro models of neurodegenerative disease. <u>Bioelectromagnetics.</u>30(7):564-72, 2009.

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. <u>Co-exposure to RF exacerbated neurotoxic effect of hydrogen peroxide in SN56</u>, but not in primary cortical neurons, whereas no cooperative effects of RF with glutamate and 25-35AA beta-amyloid were found. <u>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.</u>

## 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.

**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.

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

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. <u>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.</u>

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

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.

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] 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 (preexposure/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 Parietooccipital 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.

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

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.

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

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.

### Bolshakov MA, Alekseev SI, Bursting responses of Lymnea neurons to microwave radiation. *Bioelectromagnetics* 13(2):119-129, 1992.

Microelectrode and voltage-clamp techniques were modified to record spontaneous electrical activity and ionic currents of Lymnea stagnalis neurons during exposure to a 900-MHz field in a waveguide-based apparatus. The field was pulse-modulated at repetition rates ranging from 0.5 to 110 pps, or it was applied as a continuous wave (CW). When subjected to pulsed waves (PW), rapid, burst-like changes in the firing rate of neurons occurred at SARs of a few W/kg. If the burst-like irregularity was present in the firing rate under control conditions, irradiation enhanced its probability of occurrence. The effect was dependent on modulation, but not on modulation frequency, and it had a threshold SAR near 0.5 W/kg. CW radiation had no effect on the firing rate pattern at the same SAR. Mediator-induced, current activation of acetylcholine, dopamine, serotonin, or gamma-aminobutyric-acid receptors of the neuronal soma was not altered during CW or PW exposures and, hence, could not have been responsible for the bursting effect.

## Cao Z, Liu J, Li S, Zhao X. [Effects of electromagnetic radiation from handsets of cellular telephone on neurobehavioral function] Wei Sheng Yan Jiu 29(2):102-103, 2000. [Article in Chinese]

In order to study the effects of electromagnetic radiation from handsets of cellular telephone on neurobehavioral function, 81 staff with handsets of cellular telephone and 63 staff without handsets of cellular telephone from corporations were selected as the subjects. The subjects were investigated by questionnaire on their general health, lifestyle habit, suppress of spirit, handset using of cellular telephone, environmental exposure, morbidity, and the neurobehavioral core test battery(NCTB). The data was analyzed by chi-square, stepwise regression analysis and covariance statistics. The results showed that the average reaction time in user's group was longer than that in control group (P < 0.01). The time of using handset was negatively associated with corrected reaction number (P < 0.01). The fast reaction time and the slowest reaction time were positively associated with the length of handset using (P < 0.01, P < 0.05). The results suggested that the handset using could cause adverse health effects in neurobehavioral function.

#### D'Costa H, Trueman G, Tang L, Abdel-rahman U, Abdel-rahman W, Ong K, Cosic I. Human brain wave activity during exposure to radiofrequency field emissions from mobile phones. Australas Phys Eng Sci Med. 26(4):162-167, 2003.

The aim of this study was to determine whether there is an effect of mobile phone electromagnetic field emissions on the human electroencephalograph (EEG). EEG recordings from ten awake subjects were taken during exposure to radiofrequency (RF) emissions from a mobile phone positioned behind the head. Two experimental trials were conducted. In the first trial, RF exposures were generated by a GSM mobile phone with the speaker disabled and configured to transmit at full-radiated power. During the second trial, exposures were generated by a non-modified GSM mobile phone in active standby mode. For each trial, subjects were exposed in five minute intervals to a randomized, interrupted sequence of five active and five sham exposures. The experiment was conducted under single-blind conditions. The average EEG band power in active exposure recordings was compared to corresponding sham recordings. Statistical tests indicated significant difference in the full-power mode trial within the EEG alpha (8-13 Hz) and beta (13-32 Hz) bands. A subsequent statistical analysis of median spectral power in discrete EEG rhythms revealed significant differences in 7 of the 32 distinct frequencies overall. In conclusion, the results of this study lend support to EEG effects from mobile phones activated in talk-mode.

#### Khurana VG, Hardell L, Everaert J, Bortkiewicz A, Carlberg M, Ahonen M. Epidemiological evidence for a health risk from mobile phone base stations.Int J Occup Environ Health. 16(3):263-267, 2010.

Human populations are increasingly exposed to microwave/radiofrequency (RF) emissions from wireless communication technology, including mobile phones and their base stations. By searching PubMed, we identified a total of 10 epidemiological studies that assessed for putative health effects of mobile phone base stations. Seven of these studies explored the association between base station proximity and neurobehavioral effects and three investigated cancer. We found that eight of the 10 studies reported increased prevalence of adverse neurobehavioral symptoms or cancer in populations living at distances < 500 meters from base stations. None of the studies reported exposure above accepted international guidelines, suggesting that current guidelines may be inadequate in protecting the health of human populations. We believe that comprehensive epidemiological studies of long-term mobile phone base station exposure are urgently required to more definitively understand its health impact.

#### Hocking B, Westerman R. Neurological abnormalities associated with CDMA exposure. Occup Med (Lond) 51(6):410-413, 2001.

Dysaesthesiae of the scalp and neurological abnormality after mobile phone use have been reported previously, but the roles of the phone per se or the radiations in causing these findings have been questioned. <u>We report finding a neurological abnormality in a</u> <u>patient after accidental exposure of the left side of the face to mobile phone radiation</u> [code division multiple access (CDMA)] from a down-powered mobile phone base <u>station antenna</u>. He had headaches, unilateral left blurred vision and pupil constriction, <u>unilateral altered sensation on the forehead, and abnormalities of current perception</u> <u>thresholds on testing the left trigeminal ophthalmic nerve. His nerve function recovered</u> <u>during 6 months follow-up. His exposure was 0.015-0.06 mW/cm(2) over 1-2 h. The</u>

implications regarding health effects of radiofrequency radiation are discussed.

#### <u>Abdel-Rassoul G</u>, <u>El-Fateh OA</u>, <u>Salem MA</u>, <u>Michael A</u>, <u>Farahat F</u>, <u>El-Batanouny M</u>, <u>Salem</u> <u>E</u>. Neurobehavioral effects among inhabitants around mobile phone base stations. <u>Neurotoxicology</u>. 28(2):434-40, 2007.

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 <u>controls:</u> (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.

## 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.

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.

## 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.

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.

### Hinrichs H, Heinze HJ.Effects of GSM electromagnetic field on the MEG during an encoding-retrieval task. Neuroreport. 15(7):1191-1194, 2004.

Potential effects of GSM 1800 electromagnetic fields (EMF) on verbal memory encoding were investigated by recording event-related magnetic fields (ERMF) from the brain during subsequent memory retrieval. Twelve normal subjects participated in the study. After encoding words from a study list presented in the first phase they had to discriminate old from new words mixed together in a test list presented during the

second phase. All subjects performed two experimental sessions, one with exposure to EMF during the study phase, and one without. Exposure to EMF changed an early (350-400 ms) task-specific component of the ERMF indicating an interference of EMF and item encoding. Behavioural measures were not significantly affected. Adverse health effects cannot be derived from these data.

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

Extension of the mobile phone technology raises concern about the health effects of 900MHz 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 45min/day at a brain-averaged specific absorption rate (SAR)=1.5W/kg and for 15min/day at a SAR=6W/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 6W/kg have increased GFAP stained surface areas in the brain (p<0.05). But the chronic exposure to GSM at 1.5W/kg did not increase GFAP expression. <u>Our results indicated that chronic exposure to GSM 900MHz microwaves (SAR=6W/kg) may induce persistent astroglia activation in the rat brain (sign of a potential gliosis).</u>

## 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, 2008.

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.

#### 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.

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 shamtreated 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).

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## Barth A, Winker R, Ponocny-Seliger E, Mayrhofer W, Ponocny I, Sauter C, Vana N. A meta-analysis for neurobehavioral effects due to electromagnetic field exposure emitted by GSM mobile phones. <u>Occup Environ Med.</u>65(5):342-6, 2008.

BACKGROUND AND OBJECTIVE: Numerous studies have investigated the potential effects of electromagnetic fields (EMFs) emitted by GSM mobile phones (~900 MHz to ~1800 MHz) on cognitive functioning, but results have been equivocal. In order to try and clarify this issue, the current study carried out a meta-analysis on nineteen experimental studies. DESIGN: meta-analysis METHODS: Nineteen studies were taken into consideration. Ten of them were included in the meta-analysis as they fulfil several minimum requirements; for example, single-blind or double-blind experimental study design and documentation of means and standard deviation of the dependent variables. The meta-analysis aimed at comparing exposed with non-exposed subjects assuming that there is a common population effect so that one single effect size could be calculated. When homogeneity for single effect sizes was not given, an own population effect for each study and a distribution of population effects was assumed. RESULTS: Attention measured by the subtraction task seems to be affected in regard of decreased reaction time. Working memory measured by the N-back test seems to by affected too: Under condition 0-back target response time is lower under exposure, while under condition 2-back target response time increases. The number of errors under condition 2-back non-targets appears to be higher under exposure. CONCLUSION: Results of the meta-analysis suggest that EMFs may have a small impact on human attention and working memory.

## Papageorgiou CC, Nanou ED, Tsiafakis VG, Kapareliotis E, Kontoangelos KA, Capsalis CN, Rabavilas AD, Soldatos CR. Acute mobile phone effects on pre-attentive operation. Neurosci Lett 397(1-2):99-103, 2006.

There is a debate whether electromagnetic field (EMF) emitted by mobile phones (MP) have an effect on cognitive functions. Since the auditory P50 component of eventrelated potentials (ERPs) reflects pre-attentive processing and working memory (WM) operation, the present study was designed to investigate whether the exposure to MP-EMF affects the patterns of the P50 component of ERPs elicited during a WM test. The P50 elicited during a WM task and evoked by two warning stimuli low and high frequency (500 and 3000Hz) has been assessed in 19 normal subjects (10 women and 9 men) both without and with exposure to a 900MHz signal, emitted by a dipole antenna placed near the subjects. Results showed that the presence of MP-EMFs induced statistically significant increase in the amplitude of P50 evoked by the low frequency stimuli, at Fp1 and O1 electrode leads as compared to themselves without MP-EMF exposure. In contrast the exposure to MP-EMFs revealed statistically significant decrease of the amplitude of P50 evoked by the high frequency stimuli, at Fp1 electrode lead as compared to themselves without MP-EMF exposure. These findings provide evidence that the MP-EMF emitted by mobile phone affect pre-attentive information processing as it is reflected in P50 evoked potential. The basis of such an effect is unclear, although several possibilities exist and call for potential directions of future research.

### Papageorgiou CC, Nanou ED, Tsiafakis VG, Capsalis CN, Rabavilas AD. Gender related differences on the EEG during a simulated mobile phone signal. Neuroreport. 15(16):2557-2560, 2004.

The present study investigated the gender-related influence of electromagnetic fields (EMF), similar to that emitted by mobile phones, on brain activity. Ten women and nine men performed a short memory task (Wechsler test), both without (baseline) and with exposure to a 900 MHz signal. The EEG energy of the total waveform and the alpha, beta, delta and theta; rhythms were calculated from the recordings of 15 scalp electrodes. Baseline EEG energy of males was greater than that of females, while exposure to EMF decreased EEG energy of males and increased that of females. Memory performance was invariant to EMF exposure and gender influences. These findings indicate that EMF may exert a gender-related influence on brain activity.

#### **Effects on Brain**

Aalto S, Haarala C, Bruck A, Sipila H, Hamalainen H, Rinne JO. Mobile phone affects cerebral blood flow in humans. J Cereb Blood Flow Metab. 26(7):885-890, 2006. Mobile phones create a radio-frequency electromagnetic field (EMF) around them when in use, the effects of which on brain physiology in humans are not well known. We studied the effects of a commercial mobile phone on regional cerebral blood flow (rCBF) in healthy humans using positron emission tomography (PET) imaging. Positron emission tomography data was acquired using a double-blind, counterbalanced study design with 12 male subjects performing a computer-controlled verbal working memory task (letter 1-back). Explorative and objective voxel-based statistical analysis revealed that a mobile phone in operation induces a local decrease in rCBF beneath the antenna in the inferior temporal cortex and an increase more distantly in the prefrontal cortex. <u>Our results provide the first evidence, suggesting that the EMF emitted by a commercial mobile phone affects rCBF in humans. These results are consistent with the postulation that <u>EMF induces changes in neuronal activity.</u></u>

## 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.

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. <u>Results of the present study indicated</u>

that increased oxidative stress due to microwave exposure may contribute to cognitive impairment and inflammation in brain.

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, 2010. 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.

## 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]

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. <u>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.</u>

# 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.

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.

## 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.

**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.<u>CONCLUSION:</u> 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.

## 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.

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 FMR groups in the brain stem. <u>CONCLUSION: EMR causes to</u> <u>structural changes in the frontal cortex, brain stem and cerebellum and impair the oxidative</u> <u>stress and inflammatory cytokine system. This deterioration can cause to disease including</u> <u>loss of these areas function and cancer development.</u>

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. 2014 May 7. [Epub ahead of print] 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. <u>The relative brain weight of young rats was greatly</u> 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.

#### 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.

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. <u>Our</u> <u>results illustrated that the short-term LTE EMF exposure would modulate the</u> <u>synchronization patterns of EEG activation across the whole brain.</u>

# 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. 2013 Sep 4. pii: S1388-2457(13)00976-0. doi: 10.1016/j.clinph.2013.07.018. [Epub ahead of print]

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.

## Salford LG, Brun AR, Eberhardt JL, Malmgren L, Persson BRR, Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones. Environ Health Persp 111:881-883, 2003.

The possible risks of radio-frequency electromagnetic fields for the human body is a growing concern for the society. We have earlier shown that weak pulsed microwaves give rise to a significant leakage of albumin through the blood-brain barrier (BBB). Now we have investigated whether a pathological leakage over the BBB might be combined with damage to the neurons. Three groups of each 8 rats were exposed for 2 hours to GSM mobile phone electromagnetic fields of different strengths. We found, and present here for the first time, highly significant (p< 0.002) evidence for neuronal damage in both the cortex, the hippocampus and the basal ganglia in the brains of exposed rats.

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. 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.

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, 2013.

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  $\times$  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.

#### <u>Maby E</u>, <u>Le Bouquin Jeannes R</u>, <u>Faucon G</u>. Short-term effects of GSM mobiles phones on spectral components of the human electroencephalogram. <u>Conf Proc IEEE Eng Med</u> <u>Biol Soc.</u> 1:3751-3754, 2006.

The aim of the study was to investigate whether the GSM (global system for mobile) signals affect the electrical activity of the human brain. Nine healthy subjects and six temporal epileptic patients were exposed to radiofrequencies emitted by a GSM mobile phone signals. Electroencephalographic (EEG) signals were recorded using surface electrodes with and without radiofrequency. In order to obtain a reference, a control session was also carried out. The spectral attributes of the EEG signals recorded by surface electrodes were analyzed. The significant decrease of spectral correlation coefficients under radiofrequency influence showed that the GSM signal altered the spectral arrangement of the EEG activity for healthy subjects as well as epileptic patients. For the healthy subjects, the EEG spectral energy decreased on the studied frequency band [0-40 Hz] and more precisely on occipital electrodes for the alpha-band. For the epileptic patients, these modifications were demonstrated by an increase of the power spectral density of the EEG signal. Nevertheless, these biological effects on the EEG are not sufficient to put forward some electrophysiological hypothesis.

### 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. 2014 May 26:1743132814Y0000000392. [Epub ahead of print]

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,  $120 \pm 5$  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.

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. 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 shamexposed 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.

## **Soderqvist F**, **Carlberg M**, **Hardell L**. Mobile and cordless telephones, serum transthyretin and the blood-cerebrospinal fluid barrier: a cross-sectional study. **Environ Health.** 8(1):19, 2009.

ABSTRACT: 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(R) 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. CONCLUSIONS: 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 shortterm use, significantly higher TTR concentrations were seen in women the sooner blood was withdrawn after the most recent telephone call on that day.

# <u>Lopez-Martin E, Relova-Quinteiro JL</u>, <u>Gallego-Gomez R</u>, <u>Peleteiro-Fernandez M</u>, <u>Jorge-Barreiro FJ</u>, <u>Ares-Pena FJ</u>. GSM radiation triggers seizures and increases cerebral c-Fos positivity in rats pretreated with subconvulsive doses of picrotoxin. <u>Neurosci Lett.</u>398(1-2):139-144,2006.

This study investigated the effects of mobile-phone-type radiation on the cerebral activity of seizure-prone animals. When rats transformed into an experimental model of seizure-proneness by acute subconvulsive doses of picrotoxin were exposed to 2h GSM-modulated 900MHz radiation at an intensity similar to that emitted by mobile phones, they suffered seizures and the levels of the neuronal activity marker c-Fos in neocortex, paleocortex, hippocampus and thalamus increased markedly. Non-irradiated picrotoxin-treated rats did not suffer seizures, and their cerebral c-Fos counts were significantly lower. Radiation caused no such differences in rats that had not been pretreated with picrotoxin. We conclude that GSM-type radiation can induce seizures in rats following their facilitation by subconvulsive doses of picrotoxin, and that research should be pursued into the possibility that this kind of radiation may similarly affect brain function in human subjects with epileptic disorders.

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

We investigated the effects of mobile phone radiation on cerebral glucosemetabolism 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). <u>Our results show that short-term</u> mobile phone <u>exposure can</u> <u>locally suppress brain energy</u> metabolism in humans.

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

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 bloodbrain barrier permeability of rats 7 days after one occasion of 2h of exposure. Fortyeight 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.

### 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.

**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.

### Ragy MM. Effect of exposure and withdrawal of 900-MHz-electromagnetic waves on brain, kidney and liver oxidative stress and some biochemical parameters in male rats. Electromagn Biol Med. 2014 Apr 8. [Epub ahead of print]

Increasing use of mobile phones in daily life with increasing adverse effects of electromagnetic radiation (EMR), emitted from mobile on some physiological processes, cause many concerns about their effects on human health. Therefore, this work was designed to study the effects of exposure to mobile phone emits 900-MHz EMR on the brain, liver and kidney of male albino rats. Thirty male adult rats were randomly divided into four groups (10 each) as follows: control group (rats without exposure to EMR), exposure group (exposed to 900-MHz EMR for 1 h/d for 60 d) and withdrawal group (exposed to 900-MHz electromagnetic wave for 1 h/d for 60 d then left for 30 d without

exposure). EMR emitted from mobile phone led to a significant increase in malondialdehyde (MDA) levels and significant decrease total antioxidant capacity (TAC) levels in brain, liver and kidneys tissues. The sera activity of alanine transaminase (ALT), aspartate aminotransferase (AST), urea, creatinine and corticosterone were significantly increased (p < 0.05), while serum catecholamines were insignificantly higher in the exposed rats. These alterations were corrected by withdrawal. In conclusion, electromagnetic field emitting from mobile phone might produce impairments in some biochemicals changes and oxidative stress in brain, liver and renal tissue of albino rats.

## 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. <u>Electromagn Biol Med.</u> 31(1):67-74, 2012.

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.

#### 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.

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  $\Delta$ [O(2) Hb] and  $\Delta$ [tHb], which is small ( $\approx$ 17%) compared to a functional brain activation. A significant decrease in the medium-term response of  $\Delta$ [HHb] at 0.18 and 1.8 W/kg exposures was detected, which is in the range of physiological fluctuations. The medium-term  $\Delta$ HR was significantly higher (+1.84 bpm) at 1.8 W/kg than for sham exposure. The other parameters showed no significant effects. <u>Our results suggest that intermittent exposure to UMTS-EMF has small short- and medium-term effects on cerebral blood circulation and HR.</u>

## Persson BRR, Salford LG, Brun A, Blood-brain barrier permeability in rats exposed to electromagnetic fields used in wireless communication. Wireless Network 3:455-461, 1997.

Biological effects of radio frequency electromagnetic fields (EMF) on the blood-brain barrier (BBB) have been studied in Fischer 344 rats of both sexes. The rats were not anesthetised during the exposure. The brains were perfused with saline for 3-4 minutes, and thereafter perfusion fixed with 4% formaldehyde for 5-6 minutes. Whole coronal sections of the brains were dehydrated and embedded in paraffin and sectioned at 5 micrometers. Albumin and fibinogen were demonstrated immunochemically and classified as normal versus pathological leakage. In the present investigation we exposed male and female Fischer 344 rats in a Transverse Electromagnetic Transmission line camber to microwaves of 915 MHz as continuous wave (CW) and pulse-modulated with different pulse power and at various time intervals. The CW-pulse power varied from 0.001 W to 10 W and the exposure time from 2 min to 960 min. In each experiment we exposed 4-6 rats with 2-4 controls randomly placed in excited and nonexcited TEM cells, respectively. We have in total investigated 630 exposed rats at various modulation frequencies and 372 controls. The frequency of pathological rats is significantly increased (P< 0.0001) from 62/372 (ratio 0.17 + 0.02) for control rats to 244/630 (ratio: 0.39 + 0.043) in all exposed rats. Grouping the exposed animals according to the level or specific absorption energy (J/kg) give significant difference in all levels above 1.5 J/kg. The exposure was 915 MHz microwaves either pulse modulated (PW) at 217 Hz with 0.57 ms pulse width, at 50 Hz with 6.6 ms pulse width or continuous wave (CW). The frequency of pathological rats (0.17) among controls in the various groups is not significantly different. The frequency of pathological rats was 170/480 (0.35 + 0.03) among rats exposed to pulse modulated (PW) and 74/149 (0.50 + 0.07) among rats exposed to continuous wave exposure (CW). These results are both highly significantly different to their corresponding controls (p< 0.0001) and the frequency of pathological rats after exposure to pulsed radiation (PW) is significantly less (p< 0.002) than after exposure to continuous wave radiation (CW).

### <u>Rağbetlı MC</u>, <u>Aydinlioğlu A</u>, <u>Koyun N</u>, <u>Rağbetlı C</u>, <u>Bektas S</u>, <u>Ozdemır S</u>. The effect of mobile phone on the number of Purkinje cells: A stereological study. <u>Int J Radiat</u> <u>Biol.</u>86(7):548-54, 2010

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.

## 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.

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 16week (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.

#### Tombini M, Pellegrino G, Pasqualetti P, Assenza G, Benvenga A, Fabrizio E, Rossini PMMobile phone emissions modulate brain excitability in patients with focal epilepsy.Brain Stimul. 2012 Aug 9. [Epub ahead of print]

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.

## <u>Perentos N</u>, <u>Croft RJ</u>, <u>McKenzie RJ</u>, <u>Cvetkovic D</u>, <u>Cosic I</u>. The effect of GSM-like ELF radiation on the alpha band of the human resting EEG. <u>Conf Proc IEEE Eng Med Biol</u> Soc. 1:5680-5683, 2008.

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

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

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.

# 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.

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 doublestrand 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.

## <u>Kesari KK</u>, <u>Kumar S</u>, <u>Behari J</u>. 900-MHz microwave radiation promotes oxidation in rat brain. <u>Electromagn Biol Med.</u> 30(4):219-234, 2011.

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.

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. 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.

## Beason RC, Semm P. Responses of neurons to an amplitude-modulated microwave stimulus. Neurosci Lett 333(3):175-178, 2002.

In this study we investigated the effects of a pulsed radio frequency signal similar to the signal produced by global system for mobile communication telephones (900 MHz carrier, modulated at 217 Hz) on neurons of the avian brain. We found that such stimulation resulted in changes in the amount of neural activity by more than half of the brain cells. Most (76%) of the responding cells increased their rates of firing by an average 3.5-fold. The other responding cells exhibited a decrease in their rates of spontaneous activity Such responses indicate potential effects on humans using hand-held cellular phones.

## Ragy MM. Effect of exposure and withdrawal of 900-MHz-electromagnetic waves on brain, kidney and liver oxidative stress and some biochemical parameters in male rats. Electromagn Biol Med. 2014 Apr 8. [Epub ahead of print]

Increasing use of mobile phones in daily life with increasing adverse effects of electromagnetic radiation (EMR), emitted from mobile on some physiological processes, cause many concerns about their effects on human health. Therefore, this work was designed to study the effects of exposure to mobile phone emits 900-MHz EMR on the brain, liver and kidney of male albino rats. Thirty male adult rats were randomly divided into four groups (10 each) as follows: control group (rats without exposure to EMR), exposure group (exposed to 900-MHz EMR for 1 h/d for 60 d) and withdrawal group (exposed to 900-MHz electromagnetic wave for 1 h/d for 60 d then left for 30 d without exposure). EMR emitted from mobile phone led to a significant increase in malondialdehyde (MDA) levels and significant decrease total antioxidant capacity (TAC) levels in brain, liver and kidneys tissues. The sera activity of alanine transaminase (ALT), aspartate aminotransferase (AST), urea, creatinine and corticosterone were significantly increased (p < 0.05), while serum catecholamines were insignificantly higher in the exposed rats. These alterations were corrected by withdrawal. In conclusion, electromagnetic field emitting from mobile phone might produce impairments in some biochemicals changes and oxidative stress in brain, liver and renal tissue of albino rats.

## Maby E, Le Bouquin Jeannes R, Liegeois-Chauvel C, Gourevitch B, Faucon G.Analysis of auditory evoked potential parameters in the presence of radiofrequency fields using a support vector machines method. Med Biol Eng Comput. 42(4):562-568, 2004.

The paper presents a study of global system for mobile (GSM) phone radiofrequency effects on human cerebral activity. The work was based on the study of auditory evoked potentials (AEPs) recorded from healthy humans and epileptic patients. The protocol allowed the comparison of AEPs recorded with or without exposure to electrical fields. Ten variables measured from AEPs were employed in the design of a supervised support vector machines classifier. The classification performance measured the classifier's ability to discriminate features performed with or without radiofrequency exposure. Most significant features were chosen by a backward sequential selection that ranked

the variables according to their pertinence for the discrimination. Finally, the most discriminating features were analysed statistically by a Wilcoxon signed rank test. For both populations, the N100 amplitudes were reduced under the influence of GSM radiofrequency (mean attenuation of -0.36 microV for healthy subjects and -0.60 microV for epileptic patients). Healthy subjects showed a N100 latency decrease (-5.23 ms in mean), which could be consistent with mild, localised heating. The auditory cortical activity in humans was modified by GSM phone radiofrequencies, but an effect on brain functionality has not been proven.

## 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.

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. <u>Cell phones which spread RF may damage DNA and change gene expression in brain cells.</u>

#### 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.

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.

## Bachmann M, Lass J, Kalda J, Säkki M, Tomson R, Tuulik V, Hinrikus H. Integration of differences in EEG analysis reveals changes in human EEG caused by microwave. <u>Conf</u> Proc IEEE Eng Med Biol Soc. 1:1597-1600, 2006.

Three different methods in combination with integration of differences in signals were applied for EEG analysis to distinguish changes in EEG caused by microwave: S-parameter, power spectral density and length distribution of low variability periods. The experiments on the effect of modulated low-level microwaves on human EEG were carried out on four different groups of healthy volunteers exposed to 450 MHz microwave radiation modulated with 7 Hz, 14 Hz, 21 Hz, 40 Hz, 70 Hz, 217 or 1000 Hz frequencies. The field power density at the scalp was 0.16 mW/cm2. <u>The EEG analysis performed for individuals with three different methods showed that statistically significant changes occur in the EEG rhythms energy and dynamics between 12% and 30% of subjects.</u>

## Wang Q, Cao ZJ, Bai XT. [Effect of 900 MHz electromagnetic fields on the expression of GABA receptor of cerebral cortical neurons in postnatal rats] Wei Sheng Yan Jiu. 34(5):546-548, 2005.

OBJECTIVE: To investigate the effects of 900 MHz microwave electromagnetic fields (EMF) on the expression of neurotransmitter GABA receptor of cerebral cortical neurons in postnatal rats. METHODS: Neurons were exposed to 900 MHz continuous microwave EMF (SAR = 1.15 - 3.22mW/g) for 2 hours per day in 6 consecutive days and for 12 hours at one time. GABA receptor was chosen to be the biological end. RESULTS: Significant changes had been observed in exposed neurons in the expression of GABA receptor. (P < 0.01) <u>. CONCLUSION: The expression of GABA receptor of neurons were significantly regulated by 900 MHz microwave, and a power "window" effect was observed in the exposed neurons.</u>

#### 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.

**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.

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

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.

## Maby E, Jeannes Rle B, Faucon G. Scalp localization of human auditory cortical activity modified by GSM electromagnetic fields. Int J Radiat Biol. 82(7):465-472, 2006.

Purpose: This study attempted to determine whether there is a localized effect of GSM (Global System for Mobile communications) microwaves by studying the Auditory Evoked Potentials (AEP) recorded at the scalp of nine healthy subjects and six epileptic patients. Materials and methods: We determined the influence of GSM RadioFrequency (RF) on parameters characterizing the AEP in time or/and frequency domains. A parameter selection method using SVM (Support Vector Machines)-based criteria allowed us to estimate those most altered by the radiofrequencies. The topography of the parameter modifications was computed to determine the localization of the radiofrequency influence. A statistical test was conducted for selected scalp areas, in order to determine whether there were significant localized alterations due to the RF.Results: The epileptic patients showed a lengthening of the scalp component N100 (100 ms latency) in the frontal area contralateral to the radiation, which may be due to an afferent tract alteration. For the healthy subjects, an amplitude increase of the P200 wave (200 ms latency) was identified in the frontal area. <u>Conclusions: The present study</u>

suggests that radiofrequency fields emitted by mobile phones modify the AEP. Nevertheless, no direct link between

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

Abstract. 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.

## <u>Meral I, Mert H, Mert N, Deger Y, Yoruk I, Yetkin A, Keskin S</u>. Effects of 900-MHz electromagnetic field emitted from cellular phone on brain oxidative stress and some vitamin levels of guinea pigs. <u>Brain Res</u>1169:120-124, 2007.

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

<u>cellular phone might produce oxidative stress in brain tissue of guinea pigs.</u> However, more studies are needed to demonstrate whether these effects are harmful or/and affect the neural functions.

Mausset-Bonnefont AL, Hirbec H, Bonnefont X, Privat A, Vignon J, de Seze R.Acute exposure to GSM 900-MHz electromagnetic fields induces glial reactivity and biochemical modifications in the rat brain. Neurobiol Dis. 17(3):445-454, 2004. The worldwide proliferation of mobile phones raises the question of the effects of 900-MHz electromagnetic fields (EMF) on the brain. Using a head-only exposure device in the rat, we showed that a 15-min exposure to 900-MHz pulsed microwaves at a high brain-averaged power of 6 W/kg induced a strong glial reaction in the brain. This effect, which suggests neuronal damage, was particularly pronounced in the striatum. Moreover, we observed significant and immediate effects on the K(d) and B(max) values of N-methyl-d-aspartate (NMDA) and GABA(A) receptors as well as on dopamine transporters. Decrease of the amount of NMDA receptors at the postsynaptic membrane is also reported. Although we showed that the rat general locomotor behavior was not significantly altered on the short term, our results provide the first evidence for rapid cellular and molecular alterations in the rat brain after an acute exposure to high power GSM (Global System for Mobile communication) 900-MHz microwaves.

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. 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

<u>membrane. The fact that most of these categories are connected with membrane</u> <u>functions may have a relation to our earlier observation of albumin transport through</u> <u>brain capillaries.</u>

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

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.

#### Schirmacher A, Winters S, Fischer S, Goeke J, Galla H, Kullnick U, Ringelstein EB, Stogbauer F, Electromagnetic fields (1.8 GHz) increase the permeability to sucrose of the blood-brain barrier in vitro. Bioelectromagnetics 21(5):338-345, 2000.

We report an investigation on the influence of high frequency electromagnetic fields (EMF) on the permeability of an in vitro model of the blood-brain barrier (BBB). Our model was a co-culture consisting of rat astrocytes and porcine brain capillary endothelial cells (BCEC). Samples were characterized morphologically by scanning electron microscopy and immunocytochemistry. The BBB phenotype of the BCEC was shown by the presence of zona occludens protein (ZO-1) as a marker for tight junctions and the close contact of the cells together with the absence of intercellular clefts. Permeability measurements using (14)C-sucrose indicated a physiological tightness which correlated with the morphological findings and verified the usefulness of our in vitro model. Samples were exposed to EMF conforming to the GSM1800-standard used in mobile telephones (1.8 GHz). The permeability of the samples was monitored over four days and compared with results of samples that were cultured identically but not exposed to EMF. Exposure to EMF increased permeability for (14)C-sucrose significantly compared to unexposed samples. The underlying pathophysiological mechanism remains to be investigated.

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.

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  $\mu$ W/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).

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

Murbach, M., Neufeld, E., Christopoulou, M., Achermann, P. and Kuster, N. (2014), Modeling of EEG electrode artifacts and thermal ripples in human radiofrequency exposure studies. Bioelectromagnetics. doi: 10.1002/bem.21837.

The effects of radiofrequency (RF) exposure on wake and sleep electroencephalogram (EEG) have been in focus since mobile phone usage became pervasive. It has been hypothesized that effects may be explained by (1) enhanced induced fields due to RF coupling with the electrode assembly, (2) the subsequent temperature increase around the electrodes, or (3) RF induced thermal pulsing caused by localized exposure in the head. We evaluated these three hypotheses by means of both numerical and experimental assessments made with appropriate phantoms and anatomical human models. Typical and worst-case electrode placements were examined at 900 and 2140 MHz. Our results indicate that hypothesis 1 can be rejected, as the induced fields cause <20% increase in the 10 g-averaged specific absorption rate (SAR). Simulations with an anatomical model indicate that hypothesis 2 is also not supported, as the realistic worst-case electrode placement results in a maximum skin temperature increase of 0.31 °C while brain temperature elevations remained <0.1 °C. These local short-term temperature elevations are unlikely to change brain physiology during the time period from minutes to several hours after exposure. The maximum observed temperature ripple due to RF pulses is <0.001 °C for GSM-like signals and <0.004 °C for 20-fold higher pulse energy, and offers no support for hypothesis 3. Thus, the mechanism of interaction between RF and changes in the EEG power spectrum remains unknown.

#### Vorobyov VV, Galchenko AA, Kukushkin NI, Akoev IG, Effects of weak microwave fields amplitude modulated at ELF on EEG of symmetric brain areas in rats. Bioelectromagnetics 18(4):293-298, 1997.

Averaged electroencephalogram (EEG) frequency spectra were studied in eight unanesthetized and unmyorelaxed adult male rats with chronically implanted carbon electrodes in symmetrical somesthetic areas when a weak (0.1-0.2 mW/cm2) microwave (MW, 945 MHz) field, amplitude-modulated at extremely low frequency (ELF) (4 Hz), was applied. Intermittent (1 min "On," 1 min "Off") field exposure (10-min duration) was used. Hemispheric asymmetry in frequency spectra (averaged data for 10 or 1 min) of an ongoing EEG was characterized by a power decrease in the 1.5-3 Hz range on the left hemisphere and by a power decrease in the 10-14 and 20-30 Hz ranges on the right hemisphere. No differences between control and exposure experiments were shown under these routines of data averaging. <u>Significant elevations of EEG asymmetry in 10-14 Hz range were observed during the first 20 s after four from five onsets of the MW field,</u> when averaged spectra were obtained for every 10 s. Under neither control nor pre- and postexposure conditions was this effect observed. These results are discussed with respect to interaction of MW fields with the EEG generators.

#### 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. <u>Brain Res</u> 1346:237-246, 2010. 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 835MHz with low energy (Specific Absorption Rate: SAR=1.6W/kg) for 3months 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. Additionally, 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.

## Maby E, Jeannes RL, Faucon G, Liegeois-Chauvel C, De Seze R. Effects of GSM signals on auditory evoked responses. Bioelectromagnetics. 26(5):341-350, 2005.

The article presents a study of the influence of radio frequency (RF) fields emitted by mobile phones on human cerebral activity. Our work was based on the study of Auditory Evoked Potentials (AEPs) recorded on the scalp of healthy humans and epileptic patients. The protocol allowed us to compare AEPs recorded with or without exposure to RFs. To get a reference, a control session was also introduced. In this study, the correlation coefficients computed between AEPs, as well as the correlation coefficients between spectra of AEPs were investigated to detect a possible difference due to RFs. <u>A difference in the correlation coefficients computed in control and experimental sessions was observed, but it was difficult to deduce the effect of RFs on human health.</u>

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. 2013 Oct 18. pii: S0166-4328(13)00624-4. doi: 10.1016/j.bbr.2013.10.016. [Epub ahead of print] 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. Coexposure 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. <u>These results show that there is an impact</u> 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.

#### 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.

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. <u>Our</u> <u>results illustrated that the short-term LTE EMF exposure would modulate the</u> <u>synchronization patterns of EEG activation across the whole brain.</u>

# 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. 2013 Sep 4. pii: S1388-2457(13)00976-0. doi:

#### 10.1016/j.clinph.2013.07.018. [Epub ahead of print]

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, negative for the resting state for the formal and in left superior temporal 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. <u>CONCLUSIONS: The study provided the evidences that 30min</u> <u>LTE RF-EMF exposure modulated the spontaneous low frequency fluctuations in some brain</u> <u>regions. SIGNIFICANCE: With resting state fMRI, we found the alteration of spontaneous low</u> <u>frequency fluctuations induced by the acute LTE RF-EMF exposure.</u>

#### 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. 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 picrotoxinpretreated 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.

#### 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. 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 picrotoxinpretreated 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.

## Lebedeva NN, Sulimov AV, Sulimova OP, Kotrovskaya TI, Gailus T. Cellular phone electromagnetic field effects on bioelectric activity of human brain. *Crit Rev Biomed Eng* 28(1-2):323-337, 2000.

24 volunteers participated in the experiments. The investigation of EEG reactions to cellular phone (EMF frequency 902.4 MHz and intensity 0.06 mW/cm2) was conducted. Two experiments were performed with each subject--cellular phone exposure and Placebo Duration of the experiment was 60 min: 15 min--background; 15 min--EMF exposure or Placebo; 30 min--afterexposure. EEG was recorded in 16 standard leads with "eyes open" and "eyes closed". Special software with non-linear dynamics was developed for EEG analyses. One parameter, multichannel (global) correlation dimension, was calculated. The changes of these parameters can be evidence of brain functional state changes. As a result of EEG record processing, a significant increase of global correlation dimension during the exposure and afterexposure period was discovered, more pronounced in the case of "eyes closed". That can be viewed as the manifestation of cortex activation under phone EMF exposure.

#### Lass L, Tuulik V, Ferenets CR, Riisalo R, Hinrikus H. Effects of 7 Hz-modulated 450 MHz electromagnetic radiation on human performance in visual memory tasks. Int. J. Rad. Biol. 78: 937-944, 2002.

Abstract: Purpose: The aim was to examine low-level 7 Hz-modulated 450 MHz radiation effects on human performance in visually presented neuropsychological tasks associated with attention and short-term memory. Materials and methods: A homogeneous group of 100 subjects (37 female, 63 male) were randomly assigned to either the exposed (10-20 min, 0.158mW cm<sup>-2</sup>) or the sham-exposed group. A battery of three different tests measured attention and shortterm memory. Task 1 involved alternately selecting black digits from 1 to 25 in ascending order and white digits from 24 to 1 in descending order. The time spent on the task and the number of errors were recorded and analysed. Task 2 involved viewing a picture of 12 objects during 3 s, followed by a list of 24 words. The subject was required to select words representing previously presented objects. In task 3, an array of letters in 10 rows (60 in each row) was presented, and the subject was required to identify all examples of a particular twoletter combination. Results: The results of tasks 1 and 3 showed a significant increase in variances of errors (p < 0.05) in the exposed versus the shamexposed group. The results of task 2 indicated a significant decrease in errors (p < 0.05) in the exposed group. Conclusions: The data provide additional evidence that acute lowlevel exposure to microwaves modulated at 7 Hz can affect cognitive processes such as attention and short-term memory.

## Kramarenko AV, Tan U. Effects of high-frequency electromagnetic fields on human eeg: A brain mapping study. Int J Neurosci. 113(7):1007-1019, 2003.

Cell phones emitting pulsed high-frequency electromagnetic fields (EMF) may affect the human brain, but there are inconsistent results concerning their effects on

electroencephalogram (EEG). We used a 16-channel telemetric electroencephalograph (ExpertTM), to record EEG changes during exposure of human skull to EMF emitted by a mobile phone. Spatial distribution of EMF was especially concentrated around the ipsilateral eye adjacent to the basal surface of the brain. Traditional EEG was full of noises during operation of a cellular phone. Using a telemetric electroencephalograph (ExpertTM) in awake subjects, all the noise was eliminated, and EEG showed interesting changes: after a period of 10-15 s there was no visible change, the spectrum median frequency increased in areas close to antenna; after 20-40 s, a slow-wave activity (2.5-6.0 Hz) appeared in the contralateral frontal and temporal areas. These slow waves lasting for about one second repeated every 15-20 s at the same recording electrodes. After turning off the mobile phone, slow-wave activity progressively disappeared; local changes such as increased median frequency decreased and disappeared after 15-20 min. We observed similar changes in children, but the slow-waves with higher amplitude appeared earlier in children (10-20 s) than adults, and their frequency was lower (1.0-2.5 Hz) with longer duration and shorter intervals. The results suggested that cellular phones may reversibly influence the human brain, inducing abnormal slow waves in EEG of awake persons.

#### Krause CM, Sillanmaki L, Koivisto M, Haggqvist A, Saarela C, Revonsuo A, Laine M, Hamalainen H, Effects of electromagnetic field emitted by cellular phones on the EEG during a memory task. *Neuroreport* 11(4):761-764, 2000.

The effects of electromagnetic fields (EMF) emitted by cellular phones on the ERD/ERS of the 4-6 Hz, 6-8 Hz, 8-10 Hz and 10-12 Hz EEG frequency bands were studied in 16 normal subjects performing an auditory memory task. All subjects performed the memory task both with and without exposure to a digital 902 MHz EMF in counterbalanced order. The exposure to EMF significantly increased EEG power in the 8-10 Hz frequency band only. Nonetheless, the presence of EMF altered the ERD/ERS responses in all studied frequency bands as a function of time and memory task (encoding vs retrieval). Our results suggest that the exposure to EMF does not alter the resting EEG per se but modifies the brain responses significantly during a memory task.

#### Krause CM, Sillanmaki L, Koivisto M, Haggqvist A, Saarela C, Revonsuo A, Laine M, Hamalainen H, Effects of electromagnetic fields emitted by cellular phones on the electroencephalogram during a visual working memory task. *Int J Radiat Biol* 76(12):1659-1667, 2000.

PURPOSE: To examine the effects of electromagnetic fields (EMF) emitted by cellular phones on the event-related desynchronization/synchronization (ERD/ERS) responses of the 4-6, 6-8, 8-10 and 10-12Hz EEG frequency bands during cognitive processing. MATERIALS AND METHODS: Twenty-four subjects performed a visual sequential letter task (n-back task) with three different working memory load conditions: zero, one and two items. All subjects performed the memory task both with and without exposure to a digital 902 MHz EMF in counterbalanced order. RESULTS: The presence of EMF altered the ERD/ERS responses in the 6-8 and 8-10 Hz frequency bands but only when examined as a function of memory load and depending also on whether the presented stimulus

was a target or not. <u>CONCLUSIONS: The results suggest that the exposure to EMF</u> modulates the responses of EEG oscillatory activity approximately 8 Hz specifically during cognitive processes.

#### Krause CM, Haarala C, Sillanmaki L, Koivisto M, Alanko K, Revonsuo A, Laine M, Hamalainen H. Effects of electromagnetic field emitted by cellular phones on the EEG during an auditory memory task: a double blind replication study. Bioelectromagnetics. 25(1): 33-40, 2004.

The effects of electromagnetic fields (EMF) emitted by cellular phones on the event related desynchronization/synchronization (ERD/ERS) of the 4-6, 6-8, 8-10, and 10-12 Hz electroencephalogram (EEG) frequency bands were studied in 24 normal subjects performing an auditory memory task. This study was a systematic replication of our previous work. In the present double blind study, all subjects performed the memory task both with and without exposure to a digital 902 MHz field in a counterbalanced order. We were not able to replicate the findings from our earlier study. All eight of the significant changes in our earlier study were not significant in the present double blind replication. Also, the effect of EMF on the number of incorrect answers in the memory task was inconsistent. We previously reported no significant effect of EMF exposure on the number of incorrect answers in the memory task, but a significant increase in errors was observed in the present study. We conclude that EMF effects on the EEG and on the performance on memory tasks may be variable and not easily replicable for unknown reasons.

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. 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, preand 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. <u>The results indicated that apoptosis and</u> <u>neurodegeneration in rats exposed to EMF during pre- and postnatal periods may be</u> <u>reduced with Lycopersicon esculentum extract therapy.</u>

## <u>Krause CM</u>, <u>Pesonen M</u>, <u>Haarala Bjornberg C</u>, <u>Hamalainen H</u>. Effects of pulsed and continuous wave 902 MHz mobile phone exposure on brain oscillatory activity during cognitive processing. <u>Bioelectromagnetics.</u>28(4):296-308, 2007.

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.

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

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.

#### 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.

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.

## Ilhan A, Gurel A, Armutcu F, Kamisli S, Iraz M, Akyol O, Ozen S. Ginkgo biloba prevents mobile phone-induced oxidative stress in rat brain. Clin Chim Acta. 340(1-2): 153-162, 2004.

BACKGROUND: The widespread use of mobile phones (MP) in recent years has raised the research activities in many countries to determine the consequences of exposure to the low-intensity electromagnetic radiation (EMR) of mobile phones. Since several experimental studies suggest a role of reactive oxygen species (ROS) in EMR-induced oxidative damage in tissues, in this study, we investigated the effect of Ginkgo biloba (Gb) on MP-induced oxidative damage in brain tissue of rats. METHODS: Rats (EMR+) were exposed to 900 MHz EMR from MP for 7 days (1 h/day). In the EMR+Gb groups, rats were exposed to EMR and pretreated with Gb. Control and Gb-administrated groups were produced by turning off the mobile phone while the animals were in the same exposure conditions. Subsequently, oxidative stress markers and pathological changes in brain tissue were examined for each groups. RESULTS: Oxidative damage was evident by the: (i) increase in malondialdehyde (MDA) and nitric oxide (NO) levels in brain tissue, (ii) decrease in brain superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activities and (iii) increase in brain xanthine oxidase (XO) and adenosine deaminase (ADA) activities. These alterations were prevented by Gb treatment. Furthermore, Gb prevented the MP-induced cellular injury in brain tissue histopathologically. CONCLUSION: Reactive oxygen species may play a role in the mechanism that has been proposed to explain the biological side effects of MP, and Gb prevents the MP-induced oxidative stress to preserve antioxidant enzymes activity in brain tissue.

Ingole IV, Ghosh SK. Effect of exposure to radio frequency radiation emitted by cell phone on the developing dorsal root ganglion of chick embryo: a light microscopic study. Nepal Med Coll J. 14(4):337-341, 2012.

With an ever increasing number of cell phone users since late twenty first century, magnitude of the problem of exposure to radiation emitted by cell phone is self evident. Extensive research had been devoted to incriminate or absolve it as a health hazard. Radiofrequency radiation emitted by cell phone had been stated to be a potent carcinogen, cytotoxic, genotoxic, mutagenic and neurobehavioral teratogen. Its effect on the brain had been a subject of extensive research evidently due to its proximity to the user's brain. While considering the biological effects of radiofrequency radiation, its intensity, frequency and the duration of exposure are important determinants. Nevertheless the results of these different studies have not been unequivocal. Considering the contradictory reports, the present work was undertaken to study the effect of such an exposure on the developing neural tissue of chick embryo. The processes of cell division and differentiation are fundamental to the development of any living being and are a sensitive index of any insult sustained at this stage. Neurons of dorsal root ganglion were selected for the present study as these ganglia were fully differentiated as early as fourth day of embryonic life. By varying duration of exposure, the embryos were exposed to different doses of radiation, sacrificed at different periods of incubation and subjected to histological processing. On light microscopic study it was observed that developing neurons of dorsal root ganglion suffered a damage which was dose dependent and persisted in spite of giving the exposure-free period between two exposures.

## Haarala C, Aalto S, Hautzel H, Julkunen L, Rinne JO, Laine M, Krause B, Hamalainen H. Effects of a 902 MHz mobile phone on cerebral blood flow in humans: a PET study. Neuroreport. 14(16):2019-2023, 2003.

SUMMARY: Fourteen healthy right-handed subjects were scanned using PET with a [150]water tracer during exposure to electromagnetic field (EMF) emitted by a mobile phone and a sham-exposure under double-blind conditions. During scanning, the subjects performed a visual working memory task. Exposure to an active mobile phone produced a relative decrease in regional cerebral blood flow (rCBF) bilaterally in the auditory cortex but no rCBF changes were observed in the area of maximum EMF. It is possible that these remote findings were caused by the EMF emitted by the active mobile phone. A more likely interpretation of the present findings were a result of an auditory signal from the active mobile phone. Therefore, it is not reasoned to attribute this finding to the EMF emitted by the phone. Further study on human rCBF during exposure to EMF of a mobile phone is needed.

## Hamblin DL, Wood AW, Croft RJ, Stough C. Examining the effects of electromagnetic fields emitted by GSM mobile phones on human event-related potentials and performance during an auditory task. Clin Neurophysiol. 115(1):171-178, 2004.

OBJECTIVE: Due to the widespread use of mobile phones (MP), it is important to determine whether they affect human physiology. The aim of this study was to explore the sensitivity of auditory event-related potentials to electromagnetic emissions. METHODS: Twelve participants attended two sessions, 1 week apart. Participants performed an auditory oddball task while they were exposed to an active MP during one

session and sham exposure during the other. Each condition lasted 1 h and order was counterbalanced. N100 and P200 latencies and amplitudes were analysed for non-target waveforms, and N200 and P300 latencies and amplitudes were analysed for target waveforms. RESULTS: In real relative to sham exposure N100 amplitude and latency to non-targets were reduced, with the reduction larger over midline and right hemisphere sites. P300 latency to targets was delayed in the real exposure condition, however as this difference was greatest at left frontal and left central sites the interpretation of this result is unclear. Reaction time increased in the real relative to sham condition. No difference in accuracy was found. <u>CONCLUSIONS: The results suggest that MP exposure may affect neural activity, particularly in proximity to the phone, however caution should be applied due to the small sample size.</u>

## Gandhi OP, Lazzi G, Tinniswood A, Yu QS, Comparison of numerical and experimental methods for determination of SAR and radiation patterns of handheld wireless telephones. *Bioelectromagnetics* Suppl 4:93-101, 1999.

Some recent developments in both the numerical and experimental methods for determination of SARs and radiation patterns of handheld wireless telephones are described, with emphasis on comparison of results using the two methods. For numerical calculations, it was possible to use the Pro-Engineer CAD Files of cellular telephones for a realistic description of the device. Also, we used the expanding grid formulation of the finite-difference time-domain (FDTD) method for finer-resolution representation of the coupled region, including the antenna, and an increasingly coarser representation of the more-distant, less-coupled region. Together with the truncation of the model of the head, this procedure led to a saving of computer memory needed for SAR calculations by a factor of over 20. Automated SAR and radiation pattern measurement systems were used to validate both the calculated 1-g SARs and radiation patterns for several telephones, including some research test samples, using a variety of antennas. Even though widely different peak 1-g SARs were obtained, ranging from 0.13 to 5.41 W/kg, agreement between the calculated and the measured data for these telephones, five each at 835 and 1900 MHz, was excellent and generally within +/-20% (+/-1 dB). An important observation was that for a maximum radiated power of 600 mW at 800/900 MHz, which may be used for telephones using AMPS technology, the peak 1g SARs can be higher than 1.6 W/kg unless antennas are carefully designed and placed further away from the head.

## Frey AH, Headaches from cellular telephones: are they real and what are the implications? Environ Health Perspect 106(3):101-103, 1998.

There have been numerous recent reports of headaches occurring in association with the use of hand-held cellular telephones. Are these reported headaches real? Are they due to emissions from telephones? There is reason to believe that the answer is "yes" to both questions. There are several lines of evidence to support this conclusion. First, headaches as a consequence of exposure to low intensity icrowaves were reported in the literature 30 years ago. These were observed during the course of microwave hearing research before there were cellular telephones. Second, the blood-brain barrier

appears to be involved in headaches, and low intensity microwave energy exposure affects the barrier. Third, the dopamine-opiate systems of the brain appear to be involved in headaches, and low intensity electromagnetic energy exposure affects those systems. In all three lines of research, the microwave energy used was approximately the same--in frequencies, modulations, and incident energies—as those emitted by present day cellular telephones. <u>Could the current reports of headaches be the canary in</u> <u>the coal mine, warning of biologically significant effects?</u>

**Freude, G, Ullsperger, P, Eggert, S, Ruppe, I, Microwaves emitted by cellular telephones affect human slow brain potentials.** *Eur J Appl Physiol* **81(1-2):18-27, 2000.** The influence of electromagnetic fields (EMF) emitted by cellular telephones on preparatory slow brain potentials (SP) was studied in two experiments, about 6 months apart. In the first experiment, a significant decrease of SP was found during exposure to EMF in a complex visual monitoring task (VMT). This effect was replicated in the second experiment. In addition to the VMT, EMF effects on SP were analysed in two further, less demanding tasks: in a simple finger movement task to elicit a Bereitschaftspotential (BP) and in a two-stimulus task to elicit a contingent negative variation (CNV). In comparison to the VMT, no significant main EMF effects were found in BP and CNV tasks. <u>The results accounted for a selective EMF effect on particular aspects of human</u> <u>information processing</u>, but did not indicate any influence on human performance, wellbeing and health.

**Freude, G, Ullsperger, P, Eggert ,S, Ruppe, I, Effects of microwaves emitted by cellular phones on human slow brain potentials.** *Bioelectromagnetics* **19(6):384-387, 1998.** The influence of electromagnetic fields (EMF) emitted by cellular phones on preparatory slow brain potentials (SP) was studied in two different experimental tasks: In the first, healthy male human subjects had to perform simple self-paced finger movements to elicit a Bereitschaftspotential; in the second, they performed a complex and cognitive demanding visual monitoring task (VMT). Both tasks were performed with and without EMF exposure in counterbalanced order. Whereas subjects' performance did not differ between the EMF exposure conditions, SP parameters were influenced by EMF in the VMT<u>: EMF exposure effected a significant decrease of SPs at central and temporoparieto-occipital brain regions, but not at the frontal one. In the simple finger movement task, EMF did not affect the Bereitschaftspotential.</u>

#### Finnie JW, Blumbergs PC, Manavis J, Utteridge TD, Gebski V, Davies RA, Vernon-Roberts B, Kuchel TR. Effect of long-term mobile communication microwave exposure on vascular permeability in mouse brain. Pathology 34(4):344-347, 2002. AIMS: To study the effect of long-term exposure to global system for mobile

communication (GSM) radiofrequency fields on vascular permeability in murine brains. METHODS: Using a purpose-designed exposure system at 900 MHz, mice were given a 60-minute far-field, whole body exposure on each of 5 days perweekfor 104 weeks at specific absorption rates (SAR) of 0.25, 1.0,2.0 and 4.0 W/kg. Control mice were shamexposed or permitted free movement in a cage to evaluate any stress-related effects.

Albumin immunohistochemistry was used to detect increased vascular permeability and the efficacy of the vascular tracer was confirmed with a positive control group exposed to a clostridial toxin known to increase vascular permeability in the brain. RESULTS: In all exposed and control groups, albumin extravasation was minimal, often leptomeningeal, and was deemed insignificant as a maximum of three capillaries or venules in a given brain showed leakage from the very many blood vessels present in the three coronal brain sections. <u>CONCLUSIONS: These results suggest that prolonged exposure to mobile telephone-type radiation produces negligible disruption to blood-brain barrier integrity at the light microscope level using endogenous albumin as a vascular tracer.</u>

## <u>Ferreri F</u>, <u>Curcio G</u>, <u>Pasqualetti P</u>, <u>De Gennaro L</u>, <u>Fini R</u>, <u>Rossini PM</u>. Mobile phone emissions and human brain excitability. <u>Ann Neurol.</u>60(2):188-196, 2006.

OBJECTIVE: To test-via Transcranial Magnetic Stimulation (TMS)-the excitability of each brain hemisphere after 'real' or 'sham' exposure to the electromagnetic field (EMF) generated by a mobile phone operating in the Global System for Mobile Communication (GSM). METHODS: Fifteen male volunteers attended two experimental sessions, one week apart, in a cross-over, double-blind paradigm. In one session the signal was turned ON (EMF-on, real exposure), in the other it was turned OFF (EMF-off, sham exposure), for 45 minutes. Motor Evoked Potentials (MEPs) were recorded using a paired-pulse paradigm (testing intracortical excitability with 1 to 17 ms interstimulus intervals), both before and at different times after exposure to the EMF. Short Intracortical Inhibition (SICI) and Facilitation (ICF) curves were evaluated both on the exposed and non-exposed hemispheres. Tympanic temperature was collected during each session. RESULTS: The intracortical excitability curve becomes significantly modified during real exposure, with SICI being reduced and ICF enhanced in the acutely exposed brain hemisphere as compared to the contralateral, non-exposed hemisphere or to sham exposure. Tympanic temperature showed no significant main effect or interactions. INTERPRETATION: These results demonstrate that GSM-EMFs modify brain excitability. Possible implications and applications are discussed.

## **Fayos-Fernandez J**, <u>Arranz-Faz C</u>, <u>Martinez-Gonzalez AM</u>, <u>Sanchez-Hernandez D</u>. Effect of pierced metallic objects on sar distributions at 900 MHz. <u>Bioelectromagnetics.</u> 27(5):337-353, 2006.

. A study of the interaction between mobile phone antennas and a human head in the presence of different types of metallic objects, attached and pierced to the compressed ear, is presented in this article. Computed and measured results have been performed by considering a quasi-half-wavelength dipole as the radiating source and measurements with the DASY4 dosimetric assessment system. Two different human head models have been implemented: a homogeneously shaped sphere and a three-level head model with four different kinds of tissue. Antenna input impedance, reflection coefficient, radiation patterns, SAR distribution, absorbed power, and peak SAR values have been computed and measured for diverse scenarios, electromagnetic simulators, and organs. Despite the measuring accuracy limitations of the study, both simulated and measured results suggest that special attention has to be paid to peak

<u>SAR averaged values when wearing metallic objects close to the radiation source, since</u> <u>some increment of peak SAR averaged values is expected.</u>

#### Faucon G, <u>Le Bouquin Jeannes R</u>, <u>Maby E</u>. Short-term effects of GSM mobiles phones on spectral components of the human electroencephalogram. <u>Conf Proc IEEE Eng Med</u> <u>Biol Soc.</u> 1(1):3751-3754, 2006.

The aim of the study was to investigate whether the GSM (global system for mobile) signals affect the electrical activity of the human brain. Nine healthy subjects and six temporal epileptic patients were exposed to radiofrequencies emitted by a GSM mobile phone signals. Electroencephalographic (EEG) signals were recorded using surface electrodes with and without radiofrequency. In order to obtain a reference, a control session was also carried out. The spectral attributes of the EEG signals recorded by surface electrodes were analyzed. The significant decrease of spectral correlation coefficients under radiofrequency influence showed that the GSM signal altered the spectral arrangement of the EEG activity for healthy subjects as well as epileptic patients. For the healthy subjects, the EEG spectral energy decreased on the studied frequency band [0-40 Hz] and more precisely on occipital electrodes for the alpha-band. For the epileptic patients, these modifications were demonstrated by an increase of the power spectral density of the EEG signal. Nevertheless, these biological effects on the EEG are not sufficient to put forward some electrophysiological hypothesis.

## Eulitz, C, Ullsperger, P, Freude, G, Elbert ,T, Mobile phones modulate response patterns of human brain activity. Neuroreport 9(14):3229-3232, 1998.

Mobile phones emit a pulsed high-frequency electromagnetic field (PEMF) which may penetrate the scalp and the skull. Increasingly, there is an interest in the interaction of this pulsed microwave radiation with the human brain. Our investigations show that these electromagnetic fields alter distinct aspects of the brain's electrical response to acoustic stimuli. More precisely, our results demonstrate that aspects of the induced but not the evoked brain activity during PEMF exposure can be different from those not influenced by PEMF radiation. This effect appears in higher frequency bands when subjects process task-relevant target stimuli but was not present for irrelevant standard stimuli. As the induced brain activity in higher frequency bands has been proposed to be a correlate of coherent high-frequency neuronal activity, PEMF exposure may provide means to systematically alter the pattern fluctuations in neural mass activity.

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. 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).

#### <u>de Tommaso M</u>, <u>Rossi P</u>, <u>Falsaperla R</u>, <u>Francesco VD</u>, <u>Santoro R</u>, <u>Federici A</u>. Mobile Phones exposure induces changes of Contingent Negative Variation in humans. <u>Neurosci Lett.</u>464(2):79-83, 2009.

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 900MHz 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 10minutes 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.

#### 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. <u>Electromagn Biol</u> <u>Med.</u> 28(4):342-354, 2009.

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.

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

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.

## Chia SE, Chia HP, Tan JS, Prevalence of headache among handheld cellular telephone users in singapore: A community study. *Environ Health Perspect* 108(11):1059-1062, 2000.

We carried out a cross-sectional community study in Singapore to determine the prevalence of specific central nervous system (CNS) symptoms among hand-held cellular telephone (HP) users compared to nonusers and to study the association of risk factors and CNS symptoms among HP users. A total of 808 men and women between 12 and 70 years of age, who lived in one community, were selected using one-stage cluster random sampling and responses to a structured questionnaire. The prevalence of HP users was 44.8%. Headache was the most prevalent symptom among HP users compared to non-HP users, with an adjusted prevalence rate ratio of 1.31 [95% confidence interval, 1.00-1.70]. There is a significant increase in the prevalence of headache with increasing duration of usage (in minutes per day). <u>Prevalence of</u>

headache was reduced by more than 20% among those who used hand-free equipment for their cellular telephones as compared to those who never use the equipment. The use of HPs is not associated with a significant increase of CNS symptoms other than headache.

#### Celikozlu SD, Ozyurt MS, Cimbiz A, Yardimoglu MY, Cayci MK, Ozay Y. The effects of long-term exposure of magnetic field via 900-MHz GSM radiation on some biochemical parameters and brain histology in rats. Electromagn Biol Med. 31(4):344-355, 2012.

The aim of this study is to determine the effects of magnetic field via cell phones on some blood parameters and neurons in the brain of rats. Animals have been classified into three groups: control, Magnetic Field (MF), and F2 groups. Throughout this study, cell phones were placed on the wall of the cages. Rats were exposed to the effects of cell phones during prenatal and postnatal periods until they were 80 days old. During the study, the exposure procedure of rats was that the phone was in standby mode for a whole day and in talking mode for 30 min per day. The waves of cell phones caused an increased blood glucose level from 96.52 ± 5.64 mg/dl to 132.14 ± 5.93 mg/dl and an increased serum protein level from  $131.14 \pm 6.19$  mg/dl to  $319.29 \pm 6.73$  mg/dl compared to control. Statistically, significant differences wasn't observed in the blood cholesterol concentration between the groups compared to the control. Weekly weight gain decreased in all groups compared to the control. MF exposure decreased pyramidal neuron numbers 51.15% and increased ischemic neuron numbers 73% at cortex region of brain. In addition, vascular dilatations have increased clearly in group F2. Whereas the procedure of MF did not have any effects on hippocampal pyramidal cell numbers, magnetic fields increased the amount of ischemic neurons three-fold compared to the control. In conclusion, MF affected some biochemical parameters, especially the cortex region of the brain.

## <u>Carrubba S</u>, <u>Frilot C 2nd</u>, <u>Chesson AL Jr</u>, <u>Marino AA</u>. Mobile-phone pulse triggers evoked potentials. <u>Neurosci Lett.</u> 469(1):164-168, 2010.

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

## <u>Carballo-Quintás M</u>, <u>Martínez-Silva I</u>, <u>Cadarso-Suárez C</u>, <u>Alvarez-Figueiras M</u>, <u>Ares-Pena FJ</u>, <u>López-Martín E</u>. 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. <u>Neurotoxicology</u>. 32(4):478-494, 2011.

The acute effects of microwave exposure from the Global System for Mobile Communication (GSM) were studied in rats, using 900MHz 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, picrotoxintreated 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.

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

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, 900MHz 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.

### **Bortkiewicz A**, Gadzicka E, Szymczak W, Zmyślony M. Changes in tympanic temperature during the exposure to electromagnetic fields emitted by mobile phone. Int J Occup Med Environ Health. 25(2): 145-150, 2012.

OBJECTIVE: Mobile phones generate microwave radiation which is absorbed by exposed tissue and converted into heat. It may cause detrimental health effects. The aim of the experiment was to check if exposure to EMF emitted by mobile phone influenced the tympanic temperature.MATERIAL AND METHODS: Human volunteer study was performed on ten healthy young men, aged 22.1±4.7 years, examined three times: 1. on a day with 2×60 min of no exposure (sham day), 2. on a day with continuous, 60 min exposure and 60 min of no exposure, 3. on a day with intermittent exposure (4×15 min "on" and 4×15 min "off"). Exposure was generated by mobile phone (frequency 900 MHz, SAR 1.23 W/kg). The study was double-blind, performed under controlled conditions (at 24°C and 70% humidity). The tympanic temperature (T(ty)) was monitored every 10 sec by a thermistor probe placed close to the aural canal membrane in the ear opposite the one in contact with mobile phone (contralateral position). Multivariate repeated-measures analysis of variance was used to calculate the results.RESULTS: The mean T(ty) in the whole group during continuous exposure was significantly higher than during sham exposure (p = 0.0001). During intermittent exposure the temperature was lower than during sham day (difference was up to 0.11°C). Within an hour after continuous exposure, T(ty) was higher by 0.03°C and after intermittent exposure T(ty) was lower by 0.18°C in comparison with sham day. Two hours after exposure T(ty) was significantly lower (p = 0.0001) than after sham exposure (0.06°C and 0.26°C respectively). The trends in T(ty) during experiment differed significantly in relation to exposure conditions (p < 0.05).CONCLUSIONS: The results of this analysis indicate that the physiological response to EMF exposure from mobile phone was mostly related to type of exposure (continuous or intermittent).

Bilgici B, Akar A, Avci B, Tuncel OK. Effect of 900 MHz radiofrequency radiation on oxidative stress In rat brain and serum. Electromagn Biol Med. 32(1):20-29, 2013. The increasing use of mobile telephones raises the question of possible adverse effects of the electromagnetic fields (EMF) that these phones produce. In this study, we examined the oxidative stress in the brain tissue and serum of rats that resulted from exposure to a 900-MHz EMF at a whole body average specific absorption rate (SAR) of 1.08 W/kg for 1 h/day for 3 weeks. We also examined the antioxidant effect of garlic powder (500 mg/kg/day) given orally to EMF-exposed rats. We found that malondialdehyde (MDA) (p < 0.001) and advanced oxidation protein product (AOPP) (p < 0.05) increased in rat brain tissue exposed to the EMF and that garlic reduced these effects (p < 0.05). There was no significant difference in the nitric oxide (NO) levels in the brain. Paraoxonase (PON) was not detected in the brain. There was a significant increase in the levels of NO (p < 0.001) detected in the serum after EMF exposure, and garlic intake did not affect this increase in NO. Our results suggest that there is a significant increase in brain lipid and protein oxidation after electromagnetic radiation (EMR) exposure and that garlic has a protective effect against this oxidative stress.

## Bachmann M, Rubljova J, Lass J, Tomson R, Tuulik V, Hinrikus H. Adaptation of human brain bioelectrical activity to low-level microwave. Conf Proc IEEE Eng Med Biol Soc. 2007:4747-4750, 2007.

The experiments of adaptation of the human brain bioelectrical activity were carried out on a group of 14 healthy volunteers exposed to 450 MHz microwave radiation modulated at 40 Hz frequencies. The field power density at the scalp was 0.16 mW/cm(2). <u>Results of the study indicate that adaptation effect of human brain to lowlevel microwave exposure is evident.</u> The initial increase of EEG power was compensated and even overcompensated. The adaptation phenomena were obvious in EEG alpha and beta rhythms.

## Barcal J, Cendelín J, Vozeh F, Zalud V. Effect of whole-body exposure to high-frequency electromagnetic field on the brain electrogeny in neurodefective and healthy mice.Prague Med Rep. 106(1):91-100, 2005.

A direct registration of brain cortical and hippocampal activity during a high-frequency electromagnetic field (HF EMF) exposure was performed. All experimental procedures were done under urethane anaesthesia (20%, 2 g/kg i.p.) in Lurcher mutant mice, wild type (healthy littermates) were used as controls. Experimental animals were exposed to the HF EMF with frequency corresponding to cellular phones. Our method is based on the use of gel electrodes (silicon tubes or glass microcapillaries filled with agar) where the connection with classical electrodes is 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 the 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 p<u>hones use.</u>

## 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.

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. <u>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</u>

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). <u>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.</u>

#### 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.

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-weekold 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.

## Behari J, Kunjilwar KK, and Pyne S, Interaction of low level modulated RF radiation with Na<sup>+</sup>-K<sup>+</sup>-ATPase. Bioelectrochem Bioenerg 47:247-252, 1998.

The effect of low-level amplitude modulated radiofrequency radiation were studied on Na<sup>+</sup>-K<sup>+</sup>-ATPase activity in the brain of developing male Wistar rats of age 23 days (body weight 55-60 g). They were exposed to carrier wave (CW) frequency 147 MHz and its sub-harmonic frequencies 73.5 and 36.75 MHz amplitude modulated (AM) at 16 and 76 Hz for 30-35 days (3 h day<sup>-1</sup>, Power density 1.47 mW cm<sup>-2</sup>, average specific absorption rate 9.65-6.11 W kg<sup>-1</sup>). We observed a statistically significant increase in Na<sup>+</sup>-K<sup>+</sup>-ATPase activity in chronically exposed rats compared to the control ones. The increase in Na<sup>+</sup>-K<sup>+</sup>-ATPase activity was around 19-20% in the rats exposed to CW frequencies AM at 16 Hz compared to the controls, whereas the increase in Na<sup>+</sup>-K<sup>+</sup>-ATPase activity was around 15-16% in rats exposed to the same set of CW frequencies but AM at 76 Hz. Though there was a difference in Na<sup>+</sup>-K<sup>+</sup>-ATPase activities (3-4%) in the two groups but the difference was found to be statistically insignificant. Within the group of rats exposed to CW frequencies amplitude modulated at 16 and 76 Hz, respectively, the effect on

Na<sup>+</sup>-K<sup>+</sup>-ATPase activity was found to be independent of the magnitude of CW frequencies. An additional single short duration (20-60 min) exposure of membranes in vitro from different exposed group to the above field did not show any significant alteration on Na<sup>+</sup>-K<sup>+</sup>-ATPase activity. It is concluded that a low level effect of amplitude modulated radiation produces statistically significant effect on Na<sup>+</sup>-K<sup>+</sup>-ATPase activity but is insensitive to the carrier wave frequencies under investigation.

#### Zhou H, Su Z, Ning J, Wang C, Xie X, Qu D, Wu K, Zhang X, Pan J, Yang G. EFFECTS OF FREQUENCY, IRRADIATION GEOMETRY AND POLARISATION ON COMPUTATION OF SAR IN HUMAN BRAIN. Radiat Prot Dosimetry. 2014 Jan 6. [Epub ahead of print]

The power absorbed by the human brain has possible implications in the study of the central nervous system-related biological effects of electromagnetic fields. In order to determine the specific absorption rate (SAR) of radio frequency (RF) waves in the human brain, and to investigate the effects of geometry and polarisation on SAR value, the finite-difference time-domain method was applied for the SAR computation. An anatomically realistic model scaled to a height of 1.70 m and a mass of 63 kg was selected, which included 14 million voxels segmented into 39 tissue types. The results suggested that high SAR values were found in the brain, i.e. ~250 MHz for vertical polarisation and 900-1200 MHz both for vertical and horizontal polarisation, which may be the result of head resonance at these frequencies.

## Mausset A, de Seze R, Montpeyroux F, Privat A. Effects of radiofrequency exposure on the GABAergic system in the rat cerebellum: clues from semi-quantitative immunohistochemistry. Brain Res 912(1):33-46, 2001.

The widespread use of cellular phones raises the problem of interaction of electromagnetic fields with the central nervous system (CNS). In order to measure these effects on neurotransmitter content in the CNS, we developed a protocol of neurotransmitter detection based on immunohistochemistry and image analysis. Gamma-vinyl-GABA (GVG), an inhibitor of the GABA-transaminase was injected in rats to increase GABA concentration in the CNS. The cellular GABA contents were then revealed by immunohistochemistry and semi-quantified by image analysis thanks to three parameters: optical density (O.D.), staining area, and number of positive cells. The increase in cerebellar GABA content induced by GVG 1200 mg/kg was reflected in these three parameters in the molecular and the granular layers. Therefore, control of immunohistochemistry parameters, together with appropriate image analysis, allowed both the location and the detection of variations in cellular neurotransmitter content. This protocol was used to investigate the effects of exposure to 900 MHz radiofrequencies on cerebellar GABA content. Both pulsed emission with a specific absorption rate (SAR) of 4 W/kg and continuous emission with high SAR (32 W/kg) were tested. We observed a selective diminution of the stained processes area in the Purkinje cell layer after exposure to pulsed radiofrequency and, in addition, a decrease in O.D. in the three cell layers after exposure to continuous waves. Whether this effect is, at least partly, due to a local heating of the tissues is not known. Overall, it appears that high energetic radiofrequency exposure induces a diminution in cellular GABA content in the

#### cerebellum.

## 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.

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.

<u>The results provide further support for an effect of 2G exposures was round in any group.</u> <u>activity in young adults, but fail to support a similar enhancement in adolescents or the</u> elderly, or in any age group as a function of 3G exposure.

## Lai, H, Carino, MA, Singh, NP, Naltrexone blocks RFR-induced DNA double strand breaks in rat brain cells. Wireless Networks 3:471-476, 1997.

Previous research in our laboratory has shown that various effects of radiofrequency electromagnetic radiation (RFR) exposure on the nervous system are mediated by endogenous opioids in the brain. We have also found that acute exposure to RFR induced DNA strand breaks in brain cells of the rat. The present experiment was carried out to investigate whether endogenous opioids are also involved in RFR-induced DNA strand breaks. Rats were treated with the opioid antagonist naltrexone (1 mg/kg, IP) immediately before and after exposure **to 2450-MHz pulsed** (2 🛛 s pulses, 500 pps) RFR at a power density of 2 mW/cm2 (average whole body specific absorption rate of 1.2 W/kg) for 2 hours. DNA double strand breaks were assayed in brain cells at 4 hours after exposure using a microgel electrophoresis assay. Results showed that the RFR exposure significantly increased DNA double strand breaks in brain cells of the rat, and the effect was partially blocked by treatment with naltrexone. Thus, these data indicate that endogenous opioids play a mediating role in RFR-induced DNA strand breaks in brain cells of the rat.

## Kesari KK, Behari J, Kumar S. Mutagenic response of 2.45 GHz radiation exposure on rat brain. Int J Radiat Biol. 86(4):334-343, 2010.

Purpose: To investigate the effect of **2.45 GHz microwave radiation** on rat brain of male wistar strain. Material and methods: Male rats of wistar strain (35 days old with 130 +/- 10 g body weight) were selected for this study. Animals were divided into two groups: Sham exposed and experimental. Animals were exposed for 2 h a day for 35 days to 2.45

GHz frequency at 0.34 mW/cm(2) power density. The whole body specific absorption rate (SAR) was estimated to be 0.11 W/Kg. Exposure took place in a ventilated Plexiglas cage and kept in anechoic chamber in a far field configuration from the horn antenna. After the completion of exposure period, rats were sacrificed and the whole brain tissue was dissected and used for study of double strand DNA (Deoxyribonucleic acid) breaks by micro gel electrophoresis and the statistical analysis was carried out using comet assay (IV-2 version software). Thereafter, antioxidant enzymes and histone kinase estimation was also performed. Results: A significant increase was observed in comet head (P < 0.002), tail length (P < 0.0002) and in tail movement (P < 0.0001) in exposed brain cells. An analysis of antioxidant enzymes glutathione peroxidase (P < 0.005), and superoxide dismutase (P < 0.006) showed a decrease while an increase in catalase (P < 0.006) was observed. A significant decrease (P < 0.023) in histone kinase was also recorded in the exposed group as compared to the control (sham-exposed) ones. Oneway analysis of variance (ANOVA) method was adopted for statistical analysis. Conclusion: The study concludes that the chronic exposure to these radiations may cause significant damage to brain, which may be an indication of possible tumour promotion (Behari and Paulraj 2007).

## Lai, H, Singh, NP, Melatonin and a spin-trap compound block radiofrequency electromagnetic radiation-induced DNA strand breaks in rat brain cells. *Bioelectromagnetics* 18(6):446-454, 1997.

Effects of in vivo microwave exposure on DNA strand breaks, a form of DNA damage, were investigated in rat brain cells. In previous research, we have found that acute (2 hours) exposure to pulsed (2 microseconds pulses, 500 pps) 2450-MHz radiofrequency electromagnetic radiation (RFR) (power density 2 mW/cm2, average whole body specific absorption rate 1.2 W/kg) caused an increase in DNA single- and double-strand breaks in brain cells of the rat when assayed 4 hours post exposure using a microgel electrophoresis assay. In the present study, we found that treatment of rats immediately before and after RFR exposure with either melatonin (1 mg/kg/injection, SC) or the spin-trap compound N-tert-butyl-alpha-phenylnitrone (PBN) (100 mg/kg/injection, i.p.) blocks this effects of RFR. Since both melatonin and PBN are efficient free radical scavengers it is hypothesized that free radicals are involved in RFRinduced DNA damage in the brain cells of rats. Since cumulated DNA strand breaks in brain cells can lead to neurodegenerative diseases and cancer and an excess of free radicals in cells has been suggested to be the cause of various human diseases, data from this study could have important implications for the health effects of RFR exposure.

#### Lai H, Singh NP, Interaction of Microwaves and a Temporally Incoherent Magnetic Field on Single and Double DNA Strand Breaks in Rat Brain Cells. Electromag Biol Med 24:23-29, 2005.

The effect of a temporally incoherent magnetic field ('noise') on microwave-induced DNA single and double strand breaks in rat brain cells was investigated. Four treatment groups of rats were studied: microwave-exposure (continuous-wave **2450-MHz** 

**microwaves**, power density 1 mW/cm<sup>2</sup>, average whole body specific absorption rate of 0.6 W/kg), 'noise'-exposure (45 mG), 'microwave + noise'-exposure, and sham-exposure. Animals were exposed to these conditions for 2 hrs. DNA single and double strand breaks in brain cells of these animals were assayed 4 hrs later using a microgel electrophoresis assay. <u>Results show that brain cells of microwave-exposed rats had significantly higher levels of DNA single and double strand breaks when compared with sham-exposed animals.</u> Exposure to 'noise' alone did not significantly affect the levels (i.e., they were similar to those of the sham-exposed rats). However, simultaneous 'noise' exposure blocked microwave-induced increases in DNA strand breaks. These data indicate that simultaneous exposure to a temporally incoherent magnetic field could block microwave-induced DNA damage in brain cells of the rat.

### 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.

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 <u>conclusion, the present findings suggest that Wi-Fi exposure may exert gender-related</u> <u>alterations on neural activity associated with the amount of attentional resources</u> <u>engaged during a linguistic test adjusted to induce WM.</u>

# 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. 29(3):787-799, 2014.

Incidence rates of epilepsy and use of Wi-Fi worldwide have been increasing. TRPV1 is a Ca<sup>2+</sup> 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<sup>2+</sup> entry through activation of TRPV1 channel in epilepsy. Therefore, we tested the **effects of Wi-Fi (2.45 GHz)** exposure on Ca<sup>2+</sup> 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 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<sup>2+</sup>, 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<sup>2+</sup> increase. However, pretreatment of the neurons with CPZ, results in a protection against epilepsy-induced Ca<sup>2+</sup> influx, apoptosis and oxidative damages. In results of whole cell patch-clamp experiments, treatment of DRG with Ca<sup>2+</sup> channel antagonists [thapsigargin, verapamil + diltiazem, 2-APB, MK-801] indicated that <u>Wi-Fi exposure induced Ca<sup>2+</sup> influx via the TRPV1 channels. In conclusion, epilepsy and Wi-Fi in our experimental model is involved in Ca<sup>2+</sup> 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.</u>

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, 2013. 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)  $5.953 \times 10(-4)$  W/kg, Group III: Animals exposed to 1800 MHz at SAR 5.835  $\times$  10(-4) W/kg and Group IV: Animals exposed to 2450 MHz at SAR 6.672  $\times$  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.

#### Lai H, Carino MA, Horita A, Guy AW, Intraseptal microinjection of beta-funaltrexamine blocked a microwave-induced decrease of hippocampal cholinergic activity in the rat. *Pharmacol Biochem Behav* 53(3):613-616, 1994.

Acute (45 min) exposure to pulsed (2 microseconds pulse width, 500 pulses per second) **2450-MHz microwaves** at a power density of 1 mW/cm2 (whole body specific absorption rate 0.6 W/kg) microwaves caused a decrease in cholinergic activity in the hippocampus of the rat as measured by the sodium-dependent high-affinity choline uptake. Microinjection of beta-funaltrexamine (1 microgram) into the septum before microwave exposure blocked this effect. <u>These data indicate that mu-opioid receptors in</u>

the septum mediate a microwave-induced decrease in cholinergic activity in the hippocampus and support our hypothesis that microwaves at a whole body SAR of 0.6 W/kg can activate endogenous opioids in the brain.

# Lai H, Carino MA, Horita A, Guy AW, Single vs. repeated microwave exposure: effects on benzodiazepine receptors in the brain of the rat. *Bioelectromagnetics* 13(1):57-66, 1992.

We studied the effects of single (45 min) and repeated (ten daily 45-min sessions) microwave exposures (**2450-MHz**, 1 mW/cm2, average whole-body SAR of 0.6 W/kg, pulsed at 500 pps with pulse width of 2 microseconds) on the concentration and affinity of benzodiazepine receptors in the cerebral cortex, hippocampus, and cerebellum of the rat. We used a receptor-binding assay with 3H-flunitrazepam as ligand. <u>Immediately after a single exposure</u>, an increase in the concentration of receptor was observed in the cerebral cortex, but no significant effect was observed in the hippocampus or <u>cerebellum</u>. No significant change in binding affinity of the receptors was observed in any of the brain-regions studied. In rats subjected to repeated exposures, no significant change in receptor concentration was found in the cerebral cortex immediately after the last exposure, which may indicate an adaptation to repeated exposures. Our data also show that handling and exposure procedures in our experiments did not significantly affect benzodiazepine receptors in the brain. <u>Because benzodiazepine receptors in the brain are responsive to anxiety and stress, our data support the hypothesis that low-intensity microwave irradiation can be a source of stress.</u>

## Lai H, Carino MA, Horita A, Guy AW, Opioid receptor subtypes that mediate a microwave-induced decrease in central cholinergic activity in the rat. *Bioelectromagnetics* 13(3):237-246, 1992.

We performed experiments to investigate subtypes of opioid receptors in the brain involved in the effect of acute (45 min) pulsed microwave exposure (**2,450-MHz**, 2microseconds pulses, 500 pps, average power density 1 mW/cm2, peak-power density, 1 W/cm2, average whole body SAR 0.6 W/kg) on cholinergic activity in the rat brain. Rats were pretreated by microinjection of specific antagonists of mu, delta, and kappa opioid-receptors into the lateral cerebroventricle before exposure to microwaves. <u>The</u> <u>data showed that all three subtypes of opioid receptors are involved in the microwaveinduced decrease in cholinergic activity in the hippocampus. However, the microwaveinduced decrease in cholinergic activity in the frontal cortex was not significantly affected by any of the drug treatments, confirming our previous conclusion that the effect of microwaves on the frontal cortex is not mediated by endogenous opioids.</u>

# 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.

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. <u>Our data provide direct evidence that exposure to electromagnetic fields</u> <u>elicits a stress response in the rat hippocampus</u>.

## Lai H, Carino MA, Wen YF, Horita A, Guy AW, Naltrexone pretreatment blocks microwave-induced changes in central cholinergic receptors. *Bioelectromagnetics* 12(1):27-33, 1991.

<u>Repeated exposure of rats to pulsed, circularly polarized microwaves (2,450-MHz, 2-microseconds pulses at 500 pps, power density 1 mW/cm2, at an averaged, whole-body SAR of 0.6 W/kg) induced biphasic changes in the concentration of muscarinic cholinergic receptors in the central nervous system. An increase in receptor concentration occurred in the hippocampus of rats subjected to ten 45-min sessions of microwave exposure, whereas a decrease in concentration was observed in the frontal cortex and hippocampus of rats exposed to ten 20-min sessions. These findings, which confirm earlier work in the authors' laboratory, were extended to include pretreatment of rats with the narcotic antagonist naltrexone (1 mg/kg, IP) before each session of exposure. The drug treatment blocked the microwave-induced changes in cholinergic receptors in the brain. These data further support the authors' hypothesis that endogenous opioids play a role in the effects of microwaves on central cholinergic systems.</u>

## Lai H, Horita A, Guy AW, Microwave irradiation affects radial-arm maze performance in the rat. *Bioelectromagnetics* 15(2):95-104, 1994.

After 45 min of exposure to pulsed **2450 MHz** microwaves (2 microseconds pulses, 500 pps, 1 mW/cm2, average whole body SAR 0.6 W/kg), rats showed retarded learning while performing in the radial-arm maze to obtain food rewards, indicating a deficit in spatial "working memory" function. This behavioral deficit was reversed by pretreatment before exposure with the cholinergic agonist physostigmine or the opiate antagonist naltrexone, whereas pretreatment with the peripheral opiate antagonist naloxone methiodide showed no reversal of effect. These data indicate that both cholinergic and endogenous opioid neurotransmitter systems in the brain are involved in the microwave-induced spatial memory deficit.

## Lai H. Interaction of microwaves and a temporally incoherent magnetic field on spatial learning in the rat. Physiol Behav. 82(5):785-789, 2004.

The effect of a temporally incoherent magnetic field ('noise') on microwave-induced spatial learning deficit in the rat was investigated. Rats were trained in six sessions to locate a submerged platform in a circular water maze. Four treatment groups of rats were studied: microwave-exposure (2450-MHz continuous-wave microwaves, power density 2 mW/cm(2), average whole-body specific absorption rate 1.2 W/kg), 'noise' exposure (60 mG), 'microwave+noise' exposure, and sham exposure. Animals were exposed to these conditions for 1 h immediately before each training session. One hour after the last training session, animals were tested in a 2-min probe trial in the maze during which the platform was removed. The time spent during the 2 min in the quadrant of the maze in which the platform had been located was scored. Results show that microwave-exposed rats had significant deficit in learning to locate the submerged platform when compared with the performance of the sham-exposed animals. Exposure to 'noise' alone did not significantly affect the performance of the animals (i.e., it was similar to that of the sham-exposed rats). However, simultaneous exposure to 'noise' significantly attenuated the microwave-induced spatial learning deficit (i.e. 'microwave+noise'-exposed rats learned significantly better than the microwaveexposed rats). During the probe trial, microwave-exposed animals spent significantly less time in the quadrant where the platform was located. However, response of the 'microwave+noise'-exposed animals was similar to that of the sham-exposed animals during the probe trial. Thus, simultaneous exposure to a temporally incoherent magnetic field blocks microwave-induced spatial learning and memory deficits in the rat.

## Kesari KK, Kumar S, Behari J. Pathophysiology of microwave radiation: effect on rat brain.Appl Biochem Biotechnol. 166(2):379-388, 2012.

The study aims to investigate the effect of **2.45 GHz microwave radiation** on Wistar rats. Rats of 35 days old with  $130 \pm 10$  g body weight were selected for this study. Animals were divided into two groups: sham exposed and experimental (six animals each). Animals were exposed for 2 h a day for 45 days at 2.45 GHz frequency (power density, 0.21 mW/cm(2)). The whole body specific absorption rate was estimated to be 0.14 W/kg. Exposure took place in a ventilated plexiglas cage and kept in an anechoic chamber under a horn antenna. After completion of the exposure period, rats were killed, and pineal gland and whole brain tissues were isolated for the estimation of melatonin, creatine kinase, caspase 3, and calcium ion concentration. Experiments were performed in a blind manner and repeated. A significant decrease (P < 0.05) was recorded in the level of pineal melatonin of exposed group as compared with sham exposed. A significant increase (P < 0.05) in creatine kinase, caspase 3, and calcium ion concentration was observed in whole brain of exposed group of animals as compared to sham exposed. One-way analysis of variance method was adopted for statistical analysis. The study concludes that a reduction in melatonin or an increase in caspase-3, creatine kinase, and calcium ion may cause significant damage in brain due to chronic

exposure of these radiations. These biomarkers clearly indicate possible health implications of such exposures.

# 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.

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 theactivation 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.

### 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]

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 <u>pulsed</u> **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 costaining. The protein expressions of CDK5, p35, p25, and phosphorylated tau at Ser<sup>404</sup> 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 [ $\eta_p^2$ ]: 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<sup>404</sup> (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<sup>404</sup> (p < 0.01,  $\eta_p^2 = 0.917$ ), but did not significantly block the RF-EMF-induced apoptosis (p > 0.05,  $\eta_p^2 = 0.130$ ). <u>Conclusions: These results suggest that abnormal activity of p25/CDK5 is partially</u> <u>involved in primary cultured cortical neuron injury induced by RF-EMF exposure.</u>

# 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.

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. <u>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.</u>

## Wang, BM, Lai, H, Acute exposure to pulsed 2450-MHz microwaves affects water maze learning in the rat. Bioelectromagnetics 21:52-56, 2000.

Rats were trained in six sessions to locate a submerged platform in a circular water maze. They were exposed to pulsed **2450-MHz** microwaves (pulse width 2 🗷s, 500 pulses/s, power density 2 mW/cm2, average whole body specific absorption rate 1.2 W/kg) for 1 hr in a circular waveguide system immediately before each training session. One hour after the last training session, they were tested in a probe trial during which the platform was removed and the time spent in the quadrant of the maze in which the platform had been located during the 1-min trial was scored. Three groups of animals: microwave-exposed, sham-exposed, and cage control were studied. Data show that microwave-exposed rats were slower than sham-exposed and cage control rats in learning to locate the platform. However, there was no significant difference in swim speed among the three groups of animals, indicating that the difference in learning was not due to a change in motor functions or motivation. During the probe trial, microwave-exposed animals spent significantly less time in the quadrant that had contained the platform, and their swim patterns were different from those of the sham-exposed and cage control animals. The latter observation indicates that microwave-

exposed rats used a different strategy in learning the location of the platform. <u>These</u> results show that acute exposure to pulsed microwaves caused a deficit in spatial <u>"reference" memory in the rat.</u>

# Neubauer C, Phelan AM, Kues H, Lange DG, Microwave irradiation of rats at 2.45 GHz activates pinocytotic-like uptake of tracer by capillary endothelial cells of cerebral cortex. *Bioelectromagnetics* 11(4):261-268, 1990.

<u>Far-field exposures of male albino rats to **2.45-GHz** microwaves (10-microseconds pulses, 100 pps) at a low average power density (10 mW/cm2; SAR approximately 2 W/kg) and short durations (30-120 min) resulted in increased uptakes of tracer through the blood-brain barrier (BBB). The uptake of systemically administered rhodamineferritin complex by capillary endothelial cells (CECs) of the cerebral cortex was dependent on power density and on duration of exposure. At 5 mW/cm2, for example, a 15-min exposure had no effect. Near-complete blockade of uptake resulted when rats were treated before exposure to microwaves with a single dose of colchicine, which inhibits microtubular function. A pinocytotic-like mechanism is presumed responsible for the microwave-induced increase in BBB permeability.</u>

# 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.

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.

# Testylier G, Tonduli L, Malabiau R, Debouzy JC. Effects of exposure to low level radiofrequency fields on acetylcholine release in hippocampus of freely moving rats. Bioelectromagnetics 23:249-255, 2002.

Some central cholinergic effects have been reported in animals after acute exposure to radiofrequency electromagnetic field at low intensity. We studied acetylcholine (ACh) release in the brain of freely moving rats exposed for 1 h during the day to a **2.45 GHz** 

continuous wave radiofrequency field (RF) (2 or 4 mW/cm<sup>2</sup>) or exposed for 1 or 14 h during the night to a 800 MHz field modulated at 32 Hz (AM 200 mW/cm<sup>2</sup>). Measurements were performed by microdialysis using a membrane implanted through the upper CA1 region of the hippocampus. After irradiation with the 2.45 GHz RF, rats exposed at 2 mW/cm<sup>2</sup> did not show a significant modification of Ach release, whereas those exposed at 4 mW/cm<sup>2</sup> showed a significant 40% decrease in mean ACh release from hippocampus. This decrease was maximal at 5 h post exposure. Exposure to the 800 MHz RF for 1 h did not cause any significant effect, but exposure for 14 hrs induced a significant 43% decrease in ACh release during the period 11 p.m.-4 a.m. compared to control rats. In the control group we observed an increase of ACh release at the beginning of the night, which was linked to the waking period of rats. This normal increase was disturbed in rats exposed overnight to the 800 MHz RF. This work indicates that neurochemical modification of the hippocampal cholinergic system can be observed during and after an exposure to low intensity RF.

### 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-powerdensity microwave exposure. Physiol Behav. 106(5):631-637, 2012.

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. <u>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.</u>

## Paulraj R, Behari J. Single strand DNA breaks in rat brain cells exposed to microwave radiation. Mutat Res. 596:76-80, 2006.

This investigation concerns with the effect of low intensity microwave (**2.45** and 16.5GHz, SAR 1.0 and 2.01W/kg, respectively) radiation on developing rat brain. Wistar rats (35 days old, male, six rats in each group) were selected for this study. These animals were exposed for 35 days at the above mentioned frequencies separately in two different exposure systems. After the exposure period, the rats were sacrificed and the whole brain tissue was dissected and used for study of single strand DNA breaks by micro gel electrophoresis (comet assay). Single strand DNA breaks were measured as tail length of comet. Fifty cells from each slide and two slides per animal were observed. One-way ANOVA method was adopted for statistical analysis. This study shows that the

chronic exposure to these radiations cause statistically significant (p<0.001) increase in DNA single strand breaks in brain cells of rat.

## Paulraj R, Behari J. Protein Kinase C Activity in developing rat brain cells exposed to 2.45 GHz radiation. Electromag Biol Med 25(1) 61-70, 2006.

There is growing concern by the public regarding the potential human health hazard due to exposure to microwave frequencies. 2.45 GHz radiation widespread use in industry, research, and medicine, and leakage into the environment is possible. In order to quantitate this, experiments were performed on developing rat brain. Male Wistar 35day-old rats (n = 6) were used for this study. Animals were exposed to 2.45 GHz radiation for 2 h/day for a period of 35 days at a power density of 0.344 mW/cm<sup>2</sup> (SAR 0.11 W/kg). The control group was sham irradiated. After 35 days these rats were sacrificed and whole brain tissue was isolated for protein kinase C (PKC) assay. For morphological study the forebrain was isolated from the whole brain and PKC activity was measured using P<sup>32</sup> labeled ATP. Our study reveals a statistically significant (p < 0.05) decrease in PKC activity in hippocampus as compared to the remaining portion of the whole brain and the control group. A similar experiment conducted on hippocampus and the whole brain gave a similar result. Electron microscopic study shows an increase in the glial cell population in the exposed group as compared to the control group. This present study is indicative of a significant change after exposure to the above-mentioned field intensity. This suggests that chronic exposures may affect brain growth and development.

### Kubinyi G, Thuroczy G, Bakos J, Boloni E, Sinay H, Szabo LD, Effect of continuous-wave and amplitude-modulated 2.45 GHz microwave radiation on the liver and brain aminoacyl-transfer RNA synthetases of in utero exposed mice. *Bioelectromagnetics* 17(6):497-503, 1996.

Investigations have been carried out concerning the effects of microwave (MW) exposure on the aminoacyl-transfer ribonucleic acid (tRNA) synthetase of the progeny of females that were exposed during their entire period of gestation (19 days). The changes caused by continuous-wave (CW) and amplitude-modulated (AM) MW radiation have been compared. CFLP mice were exposed to MW radiation for 100 min each day in an anechoic room. The MW frequency was 2.45 GHz, and the amplitude modulation had a 50 Hz rectangular waveform (on/off ratio, 50/50%). The average power density exposure was 3 mW/cm2, and the whole body specific absorption rate (SAR) was 4.23 +/- 0.63 W/kg. The weight and mortality of the progeny were followed until postnatal day 24. Aminoacyl-tRNA synthetase enzymes and tRNA from the brains and livers of the offspring (461 exposed, 487 control) were isolated. The aminoacyltRNA synthetase activities were determined. The postnatal increase of body weight and organ weight was not influenced by the prenatal MW radiation. The activity of enzyme isolated from the brain showed a significant decrease after CW MW exposure, but the changes were not significant after 50 Hz AM MW exposure. The activity of the enzyme isolated from liver increased under CW and 50 Hz modulated MW.

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

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 <u>+</u> 3.10<sup>-3,</sup> 0.069 <u>+</u> 5.10<sup>-3</sup>, 0.27 <u>+</u> 21.10<sup>-3</sup> 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 a 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.

Gürler HS, Bilgici B, Akar AK, Tomak L, Bedir A. Increased DNA oxidation (8-OHdG) and protein oxidation (AOPP) by Low level electromagnetic field (2.45 GHz) in rat brain and protective effect of garlic. Int J Radiat Biol. 2014 May 21:1-15. [Epub ahead of print] Purpose: To investigate the oxidative damage and protective effect of garlic on rats exposed to low level of electromagnetic fields (EMF) at 2.45 GHz Microwave radiation (MWR). Methods: Thirty six Wistar rats were divided into three groups. Group I was the control group and not exposed to EMF. Group II and III were exposed to low level EMF (3.68±0.36 V/m) at 2.45 GHz MWR for 1 hour/day for 30 consecutive days. Daily 500 mg/kg garlic was given to Group III during the study period. At the end of the study, thiobarbituric acid reactive substances (TBARS), advanced oxidation protein products (AOPP) and 8-hydroxydeoxyguanosine (8-OHdG) levels were investigated in brain tissue and blood samples. Results: Exposure to low level of EMF increased 8-OHdG level in both plasma and brain tissue whereas it increased AOPP level only in plasma. Garlic prevented the increase of 8-OHdG level in brain tissue and plasma AOPP levels. Conclusions: It may be concluded that low level EMF at 2.45 GHz MWR increases the DNA damage in both brain tissues and plasma of the rats whereas it increases protein

oxidation only in plasma. It may also be argued that the use of garlic decreases these effects.

# Fukui Y, Hoshino K, Inouye M, Kameyama Y, Effects of hyperthermia induced by microwave irradiation on brain development in mice. *J Radiat Res (Tokyo)* 33(1):1-10, 1992.

Pregnant mice were exposed to **2.45 GHz of microwave** radiation for 15 or 20 min on day 13 of gestation. The highest maternal core temperature during the exposure did not exceed 42.5 degrees C. Pregnant females also were immersed in hot water at 42 degrees C for 15 min to compare thermal effects on brain development. Animals were killed 9 hours after treatment, and the pyknotic cells in the ventricular zone of telencephalon were counted. The respective incidences of these cells in the groups exposed to microwaves for 15 and 20 min were 1.83% and 3.06%. Microwave radiation for 20 min had an effect that was comparable to that of immersion in 42 degrees C hot water for 15 min. In addition, some animals were examined on day 18 of gestation, and some of their offspring were examined at 6 weeks of age in an examination of long-term effects. Brain weight for the group, and the numerical density of the neurons in the cerebrum was higher. We concluded that microwave radiation at the dose tested mainly has a thermal effect.

### 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.

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, <u>Melatonin supplementation in DRG neurons and brain seems to have</u> <u>protective effects on the 2.45 GHz-induced increase Ca(2+) influx, EEG records and cell</u> <u>viability of the hormone through TRPM2 and voltage gated Ca(2+) channels.</u>

Field AS, Ginsburg K, Lin JC The effect of pulsed microwaves on passive electrical properties and interspike intervals of snail neurons. *Bioelectromagnetics* 14(6):503-520, 1993.

The effects of pulsed microwaves (2.45 GHz, 10 microseconds, 100 pps, SAR: 81.5 kW/kg peak, 81.5 W/kg average) on membrane input resistance and action potential (AP) interval statistics were studied in spontaneously active ganglion neurons of land snails (Helix aspersa), at strictly constant temperature (20.8 +/- .07 degrees C worst case). Statistical comparison with sham-irradiated neurons revealed a significant increase in the mean input resistance of neurons exposed to pulsed microwaves (P < or = .05). Pulsed microwaves had no visible effect on mean AP firing rate; this observation was confirmed by analysis of interspike intervals (ISIs). Using an integrator model for spontaneously active neurons, we found the net input current to be more variable in neurons exposed to pulsed microwaves. The mean input current was not affected. The standard deviation of ISIs and the autocorrelation of the input current were marginally affected, but these changes were not consistent across neurons. Although the observed effects were less obvious than those reported in other studies, they represent evidence of a direct interaction between neurons and pulsed microwaves, in the absence of macroscopic temperature changes. The data do not suggest a single, specific mechanism for such interaction.

# Ding G, Xie X, Zhang L et al. Changes of nitric oxide synthase in hippocampus and cerebellum of the rat following exposure to electromagnetic pulse. Chin J Phys Med 20:81-83, 1998.

Objective: In order to explore the role of nitric oxide in the obstruction of learning and memory of the rat caused by exposing to electromagnetic pulses (EMP), the distribution of nitric oxide synthase (NOS) expression was studied in hippocampus and cerebellum of the rat following exposure to EMP. Methods: SP immunohistochemical staining was employed to detect the distribution of NOS expression. Results: The number of NOS positive neurons and the intensity of positive staining in hippocampus were decreased at 1.5 and 24 h after exposure to EMP. At 48 h, the number of NOS positive neurons reversed to control level but the intensity of positive staining was still low. the expression of NOS in cerebellum had no obvious changes. <u>Conclusion: Decrease of NOS expression in hippocampus relates to the obstruction of learning and memory of the rat after exposure to EMP.</u>

## Lange DG, Sedmak J, Japanese encephalitis virus (JEV): potentiation of lethality in mice by microwave radiation. *Bioelectromagnetics* 12(6):335-348, 1991.

The expression of Japanese Encephalitis Virus (JEV) lethality in mice requires entry of the virus into the central nervous system. This entry is presumably through the capillary endothelial cells (CEC), because entry between CECs is inhibited by bands of circumferential tight-junctions. A viremic stage occurs during the first 4 to 5 days after JEV administration in mice, and both microwave **radiation (2.45-GHz, continuous wave, 10-min exposure)** and hypercarbia were employed to increase CEC permeability to JEV. Exposure to microwaves at power densities of 10-50 mW/cm2 resulted in a dose-dependent increase in JEV-induced lethality. Mice did not become tolerant or sensitized to microwave potentiation of JEV-induced mortality because 4 daily exposures at 10 or 50 mW/cm2 (SARS, approximately 24-98 W/kg) did not alter the lethality pattern to

subsequent microwave radiation of JEV-exposed animals. Similarly, hypercarbia (5, 10, and 20% CO2) was observed to produce a dose-dependent increase in JEV-induced lethality. Both microwave radiation and hypercarbia are thought to promote pinocytosis in CNS capillary endothelial cells. This may be one mechanism by which they enhance JEV-induced lethality in adult Swiss-Cox mice.

# Inaba R, Shishido K, Okada A, Moroji T. Effects of whole body microwave exposure on the rat brain contents of biogenic amines. Eur J Appl Physiol Occup Physiol. 65(2):124-128, 1992.

The effects of whole body microwave exposure on the central nervous system (CNS) of the rat were investigated. Rats weighing from 250 to 320 g were exposed for 1 h to whole body microwave with a frequency of 2450 MHz at power densities of 5 and 10 mW.cm-2 at an ambient temperature of 21-23 degrees C. The rectal temperatures of the rats were measured just before and after microwave exposure and mono-amines and their metabolites in various discrete brain regions were determined after microwave exposure. Microwave exposure at power densities of 5 and 10 mW.cm-2 increased the mean rectal temperature by 2.3 degrees C and 3.4 degrees C, respectively. The noradrenaline content in the hypothalamus was significantly reduced after microwave exposure at a power density of 10 mW.cm-2. There were no differences in the dopamine (DA) content of any region of the brain between microwave exposed rats and control rats. The dihydroxyphenyl acetic acid (DOPAC) content, the main metabolite of DA, was significantly increased in the pons plus medulla oblongata only at a power density of 10 mW.cm-2. The DA turnover rates, the DOPAC:DA ratio, in the striatum and cerebral cortex were significantly increased only at a power density of 10 mW.cm-2. The serotonin (5-hydroxytryptamine, 5-HT) content in all regions of the brain of microwave exposed rats was not different from that of the control rats. The 5-hydroxyindoleacetic acid (5-HIAA) content in the cerebral cortex of microwave exposed rats was significantly increased at power densities of 5 and 10 mW.cm-2.

# 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.

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. <u>RESULTS: The cortex brain vitamin A (p < 0.05), vitamin C (p < 0.01) and vitamin E (p < 0.05) concentrations were increased by</u>

<u>selenium and L-carnitine supplementation. Lipid peroxidation, levels were lower in</u> <u>group C (p < 0.05) and D (p < 0.01) than in group B where as reduced glutathione levels</u> <u>were higher in group C (p < 0.05) than in group A1, A2 and B. However, B-carotene</u> <u>levels did not change in the five groups.</u> CONCLUSIONS<u>: L-carnitine and selenium seem</u> <u>to have protective effects on the 2.45 GHz-induced decrease of the vitamins by</u> <u>supporting antioxidant redox system. L-carnitine on the vitamin concentrations seems</u> <u>to more protective affect than in selenium.</u>

De Roos AJ, Teschke K, Savitz DA, Poole C, Grufferman S, Pollock BH, Olshan AF. Parental occupational exposures to electromagnetic fields and radiation and the incidence of neuroblastoma in offspring. Epidemiology 12(5):508-517, 2001. We examined parental occupational exposures to electromagnetic fields and radiation and the incidence of neuroblastoma in offspring. Cases were 538 children diagnosed with neuroblastoma between 1992 and 1994 in the United States or Canada. Agematched controls were selected by random-digit dialing. Occupational exposures to electrical equipment and radiation sources were classified by an industrial hygienist, and average exposures to extremely low frequency magnetic fields were estimated using a job exposure matrix. Maternal exposure to a broad grouping of sources that produce radiofrequency radiation was associated with an increased incidence of neuroblastoma (odds ratio = 2.8; 95% confidence interval = 0.9-8.7). Paternal exposure to batterypowered forklifts was positively associated with neuroblastoma (odds ratio = 1.6; 95% confidence interval = 0.8-3.2), as were some types of equipment that emit radiofrequency radiation (odds ratios congruent with 2.0); however, the broad groupings of sources that produce ELF fields, radiofrequency radiation, or ionizing radiation were not associated with neuroblastoma. Paternal average extremely low frequency magnetic field exposure >0.4 microTesla was weakly associated with neuroblastoma (odds ratio = 1.6; 95% confidence interval = 0.9-2.8), whereas maternal exposure was not. Overall, there was scant supportive evidence of strong associations between parental exposures in electromagnetic spectrum and neuroblastoma in offspring.

### **Central Nervous System Effects**

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

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 highly 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 24h 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. Consistent 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 in the brain. <u>Together</u>, these results suggested that 1800 MHz RF radiation could cause <u>oxidative damage to mtDNA in primary cultured neurons</u>. Oxidative damage to mtDNA <u>may account for the neurotoxicity of RF radiation in the brain</u>.

## Pakhomov AG, [Non-thermal microwave effect on nerve fiber function]. *Biofizika* 38(2):367-371, 1993. [Article in Russian]

Effects of microwave radiation (915 MHz, PW, peak SAR 20-30 W/g, pulse duration 1 mcs, 50.000 and 25.000 p.p.s.) were investigated in isolated frog nerve cord preparation. Nerve VHF heating didn't exceed 2.2 degrees C due to intense Ringer's solution perfusion. It was established that nerve irradiation simultaneously with its stimulation lead to significant decrease of action potential amplitude and peak latency. Since the equal conventional heating of the nerve caused the opposite changes (amplitude increase), the results obtained argue for non-thermal mechanism of microwave action.

# <u>Schüz J</u>, <u>Waldemar G</u>, <u>Olsen JH</u>, <u>Johansen C</u>. Risks for central nervous system diseases among mobile phone subscribers: a Danish retrospective cohort study. <u>PLoS One.</u> 4(2):e4389, 2009

The aim of this study was to investigate a possible link between cellular telephone use and risks for various diseases of the central nervous system (CNS). We conducted a large nationwide cohort study of 420 095 persons whose first cellular telephone subscription was between 1982 and 1995, who were followed through 2003 for hospital contacts for a diagnosis of a CNS disorder. Standardized hospitalization ratios (SHRs) were derived by dividing the number of hospital contacts in the cohort by the number expected in the Danish population. The SHRs were increased by 10-20% for migraine and vertigo. No associations were seen for amyotrophic lateral sclerosis, multiple sclerosis or epilepsy in women. SHRs decreased by 30-40% were observed for dementia (Alzheimer disease, vascular and other dementia), Parkinson disease and epilepsy among men. In analyses restricted to subscribers of 10 years or more, the SHRs remained similarly increased for migraine and vertigo and similarly decreased for Alzheimer disease and other dementia and epilepsy (in men); the other SHRs were close to unity. In conclusion, the excesses of migraine and vertigo observed in this first study on cellular telephones and CNS disease deserve further attention. An interplay of a healthy cohort effect and reversed causation bias due to prodromal symptoms impedes detection of a possible association with dementia and Parkinson disease. Identification of the factors that result in a healthy cohort might be of interest for elucidation of the etiology of these diseases.

### Hardell L, <u>Söderqvist F</u>, <u>Carlberg M</u>, <u>Zetterberg H</u>, <u>Mild KH</u>. Exposure to wireless phone emissions and serum beta-trace protein. <u>Int J Mol Med.</u> 26(2):301-306, 2010.

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 betatrace 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 downregulate 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.

# Hamann W, Abou-Sherif S, Thompson S, Hall S. Pulsed radiofrequency applied to dorsal root ganglia causes a selective increase in ATF3 in small neurons. <u>Eur J Pain.</u> 10(2):171-176, 2006.

BACKGROUND: This is a "proof of concept study" to test the hypothesis that pulsed radiofrequency, PRF, produces cell stress at the primary afferent level without signs of overt thermal damage. We assumed that cell stress would result in impairment of normal function, and used the expression of activating transcription factor 3, ATF3, as an indicator of cellular "stress". METHODS: PRF (20ms of 500-kHz RF pulses, delivered at a rate of 2Hz; maximum temperature 42 degrees C) was delivered either to the sciatic nerve of adult rats in mid thigh, or to the L4 anterior primary ramus just distal to the intervertebral foramen. Controls were sham-operated or L4 axotomised. All tissues were examined 14 days after surgery. The percentage of CGRP- or ATF3-positive DRG neuronal somata was calculated using image analysis software (SigmaScan Pro 4). RESULTS: ATF3 expression was upregulated in L4 DRG neuronal cell bodies, irrespective of their size, after axotomy. It was also upregulated significantly (p<0.002) and selectively, in small and medium calibre L4 DRG neurons, when PRF was applied close to the DRG just distal to the intervertebral foramen. PRF did not produce any obvious cellular changes in the nerve or L4 DRG neurons when applied to the sciatic nerve in mid-thigh. CONCLUSION: PRF has a biological effect, unlikely to be related to overt thermal damage. It appears to be selective in that it targets the group of neurons whose axons are the small diameter C and Adelta nociceptive fibres.

# 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.

**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.

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. 2013 Aug 1. doi: 10.1002/bem.21805. [Epub ahead of print] 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.

## Xu S, Ning W, Xu Z, Zhou S, Chiang H, Luo J. Chronic exposure to GSM 1800-MHz microwaves reduces excitatory synaptic activity in cultured hippocampal neurons. <u>Neurosci Lett.</u>398(3):253-257,2006.

The world wide proliferation of mobile phones raises the concern about the health effects of 1800-MHz microwaves on the brain. The present study assesses the effects of microwave exposure on the function of cultured hippocampal neurons of rats using whole cell patch-clamp analysis combined with immunocytochemistry. We showed that chronic exposure (15min per day for 8 days) to Global System for Mobile Communication (GSM) 1800-MHz microwaves at specific absorption rate (SAR) of 2.4W/kg induced a selective decrease in the amplitude of alpha-amino-3-hydroxy-5-methyl-4-soxazole propionic acid (AMPA) miniature excitatory postsynaptic currents (mEPSCs), whereas the frequency of AMPA mEPSCs and the amplitude of N-methyl-d-aspartate (NMDA) mEPSCs did not change. Furthermore, the GSM microwave treatment decreased the expression of postsynaptic density 95 (PSD95) in cultured neurons. Our results indicated that 2.4W/kg GSM 1800-MHz microwaves may reduce excitatory synaptic activity and the number of excitatory synapses in cultured rat hippocampal neurons.

## Barteri M, Pala A, Rotella S. Structural and kinetic effects of mobile phone microwaves on acetylcholinesterase activity. Biophys Chem. 113(3):245-253, 2005.

The present study provides evidence that "in vitro" simple exposure of an aqueous solution of electric eel acetylcholinesterase (EeAChE; EC 3.1.1.7.) to cellular phone emission alters its enzymatic activity. <u>This paper demonstrates</u>, by combining different experimental techniques, that radio frequency (RF) radiations irreversibly affect the structural and biochemical characteristics of an important CNS enzyme. These results were obtained by using a commercial cellular phone to reproduce the reality of the human exposition. This experimental procedure provided surprising effects collected practically without experimental errors because they were obtained comparing native and irradiated sample of the same enzyme solution. Although these results cannot be used to conclude whether exposure to RF during the use of cellular phone can lead to any hazardous health effect, they may be a significant first step towards further verification of these effects on other "ex vivo" or "in vivo" biological systems.

# Acar GO, Yener HM, Savrun FK, Kalkan T, Bayrak I, Enver O. Thermal effects of mobile phones on facial nerves and surrounding soft tissue. Laryngoscope. 119(3):559-562, 2009.

OBJECTIVE: To investigate the possible thermal effects of microwaves from mobile phones on **facial nerves (FN)** and surrounding soft tissue. STUDY DESIGN:: A prospective study. METHODS: We studied FN conduction rate and compound muscle action potentials (CMAP) on 12 rabbits before exposure to radiofrequency radiation (RFR) emitted from a mobile phone. Also, the temperature change in the soft tissues around the FN was investigated by a four channel Luxtron fiber optic system. A mobile phone with 1900 MHz frequency was placed over the ipsilateral ear of the rabbit for 25 minutes, and FN and surrounding tissues were exposed to a 1.5 watts pulse modulated

(217 packets/s) electromagnetic field. During exposure to RFR, immediately after turning off the mobile phone, and 25 minutes after the exposure temperature change in the surrounding tissue of the FN was recorded and compared to preexposure values. Additionally, another recording regarding the FN functions was done and the data were compared to preexposure values. RESULTS: The average temperature of the surrounding soft tissues was 0.39 K higher than the preexposure values during the exposure and immediately after turning off the mobile phone, and decreased to normal levels 25 minutes after the exposure, which was statistically significant. The amplitudes of FN CMAP after radiofrequency radiation exposure were significantly smaller than the preexposure amplitudes and the amplitudes were normal in the 25 minute measurement. CONCLUSION: The RFR emitted from a mobile phone can cause temporary FN dysfunction that can be due to temporary temperature increase in the soft tissue around the FN.

### Ersan Odacı, Ayşe İkinci, Mehmet Yıldırım, Haydar Kaya, Metehan Akça, Hatice Hancı, Osman Fikret Sönmez, Ali Aslan, Mukadder Okuyan, Orhan Baş 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.

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.

# 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.

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 proinflammatory 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 proinflammatory responses in astrocytes and microglia, characterized by different expression and release profiles of IL-1 $\beta$ , TNF- $\alpha$ , 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.

### 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]

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

## Ivanova VIu, Martynova OV, Aleinik SV, Limarenko AV. [Effect of modified SHF and acoustic stimulation on spectral characteristics of the electroencephalograms of the

### cat brain] Biofizika. 45(5):935-940, 2000. [Article in Russian]

The effect of modulated electromagnetic fields on the spectral parameters of bioelectric brain activity in awake cats was studied by registering the electroencephalogram from the skin surface in the vertex area using carbon electrodes. In the normal electroencephalogram, spectral components in the range above 20 Hz predominated. It was shown that, upon irradiation with electromagnetic field (basic frequency 980 MHz, power density 30-50 microW/cm2), spectral components in the range of 12-18 Hz begin to prevail. A similarity in the redistribution of the power of spectral components upon both acoustic and modulated electromagnetic influences was revealed. The results suggest that there is a a common neurophysiological mechanism by which modulated electromagnetic stimulation affect the electrical activity of the brain. This ia consistent with the assumption that the effect of the electromagnetic field on the central nervous system is mediated through the acoustic sensory system.

## Verma M, Dutta SK. Microwave induced alteration in the neuron specific enolase gene expression. Cancer Biochem Biophys. 13(4):239-244, 1993.

Exposure of pNGE7, a recombinant clone containing the coding and regulatory sequences for the expression of neuron specific enolase gene, cells to electromagnetic radiations (915 MHz, 16 Hz AM, SAR 0.05 mW/kg) resulted in the elevation of neuron specific enolase (NSE), a diagnostic marker for neuron and lung cancer. Using ionexchange chromatography we separated the neuron specific enolase activity from the non-neuronal enolase (NNE) activity and observed an alteration in the expression of neuron specific enolase and non-neuronal enolase. The clinical applications of the present studies have been discussed.

Khudnitskii, SS, Moshkarev, EA, Fomenko, TV, [On the evaluation of the influence of cellular phones on their users]. [Article in Russian] Med Tr Prom Ekol (9):20-24, 1999. The authors studied influence of ultrahigh frequency radiation caused by cellular phones on functional state of central nervous, cardiovascular systems and local temperature changes in cellular phones users. The head area near the phone antenna appeared to be under the most intensive heating. <u>Ultrahigh frequency radiation induces significant</u> changes in local temperature and in physiologic parameters of central nervous and cardiovascular systems.

#### 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.

<u>Radiofrequency electromagnetic fields (EMF) are harmful to public health, but the</u> <u>certain anti-irradiation mechanism is not clear yet.</u> 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 irradiationinduced injury on the cultured rat cortical neurons.

### Ivaschuk OI, Jones RA, Ishida-Jones T, Haggren W, Adey WR, Phillips JL, Exposure of nerve growth factor-treated PC12 rat pheochromocytoma cells to a modulated radiofrequency field at 836.55 MHz: effects on c-jun and c-fos expression. Bioelectromagnetics 18(3):223-229, 1997.

Rat PC12 pheochromocytoma cells have been treated with nerve growth factor And then exposed to athermal levels of a packet-modulated radiofrequency field At 836.55 MHz. This signal was produced by a prototype time-domain multiple-access (TDMA) transmitter that conforms to the North American digital cellular telephone standard. Three slot average power densities were used: 0.09, 0.9, and 9 mW/cm2. Exposures were for 20, 40, and 60 min and included an intermittent exposure regimen (20 min on/20 min off), resulting in total incubation times of 20, 60, and 100 min, respectively. Concurrent controls were sham exposed. After extracting total cellular RNA, Northern blot analysis was used to assess the expression of the immediate early genes, c-fos and c-jun, in all cell populations. No change in c-fos transcript levels were detected after 20 min exposure at each field intensity (20 min was the only time period at which c-fos message could be detected consistently). Transcript levels for c-jun were altered only after 20 min exposure to 9 mW/cm2 (average 38% decrease).

### <u>Joubert V</u>, <u>Bourthoumieu S</u>, <u>Leveque P</u>, <u>Yardin C</u>. Apoptosis is Induced by Radiofrequency Fields through the Caspase-Independent Mitochondrial Pathway in Cortical Neurons. <u>Radiat Res.</u> 169(1):38-45, 2008.

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. <u>Our results show that,</u> <u>under the experimental conditions used, exposure of primary rat neurons to CW RF</u> <u>fields may induce a caspase-independent pathway to apoptosis that involves AIF.</u>

# Seaman RL, Phelix CF. Acute effects of pulsed microwaves and 3-nitropropionic acid on neuronal ultrastructure in the rat caudate-putamen. Bioelectromagnetics. 26(2):82-101, 2005.

Ultrastructure of the medium sized "spiny" neuron in rat dorsal-lateral caudateputamen was assessed after administration of 3-nitropropionic acid (3-NP) and exposure to pulsed microwaves. Sprague-Dawley male rats were given two daily intraperitoneal doses of 0 or 10 mg/kg 3-NP and 1.5 h after each dose were exposed to microwave radiation at a whole body averaged specific absorption rate (SAR) of 0 (sham exposure), 0.6, or 6 W/kg for 30 min. Microwave exposure consisted of 1.25 GHz radiation delivered as 5.9 mus pulses with repetition frequency 10 Hz. Tissue samples taken 2-3 h after the second sham or microwave exposure showed no injury with light microscope methods. Blinded qualitative assessment of ultrastructure of randomly selected neurons from the same samples did reveal differences. Subsequent detailed, guantitative measurements showed that, when followed by sham exposure, administration of 3-NP significantly increased endoplasmic reticulum (ER) intracisternal width, ER area density, and nuclear envelope thickness. Microwave exposure at 6 W/kg alone also significantly increased these measures. Exposure of 3-NP treated animals at 6 W/kg significantly increased effects of 3-NP on ultrastructure. Although exposure at 0.6 W/kg alone did not affect ultrastructure measures, exposure of 3-NP treated animals at 0.6 W/kg reduced the effects of 3-NP. We concluded that 3-NP changed neuronal ultrastructure and that the microwave exposures used here changed neuronal ultrastructure in ways that depended on microwave SAR and neuron metabolic status. The apparent cancellation of 3-NP induced changes by exposure to pulsed microwaves at 0.6 W/kg indicated the possibility that such exposure can protect against the effects of mitochondrial toxins on the nervous system.

Zhou H, Su Z, Ning J, Wang C, Xie X, Qu D, Wu K, Zhang X, Pan J, Yang G. EFFECTS OF FREQUENCY, IRRADIATION GEOMETRY AND POLARISATION ON COMPUTATION OF SAR IN HUMAN BRAIN. Radiat Prot Dosimetry. 2014 Jan 6. [Epub ahead of print] The power absorbed by the human brain has possible implications in the study of the central nervous system-related biological effects of electromagnetic fields. In order to determine the specific absorption rate (SAR) of radio frequency (RF) waves in the human brain, and to investigate the effects of geometry and polarisation on SAR value, the finite-difference time-domain method was applied for the SAR computation. An anatomically realistic model scaled to a height of 1.70 m and a mass of 63 kg was selected, which included 14 million voxels segmented into 39 tissue types. The results suggested that high SAR values were found in the brain, i.e. ~250 MHz for vertical polarisation and 900-1200 MHz both for vertical and horizontal polarisation, which may be the result of head resonance at these frequencies.

# 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. 2012 Feb 24. [Epub ahead of print]

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.

## **Esen F**, **Esen H**Effect of electromagnetic fields emitted by cellular phones on the latency of evoked electrodermal activity. <u>Int J Neurosci.</u> 116(3):321-329, 2006.

The widespread use of cellular phones raises the question of their possible adverse biological effects, especially on the central nervous system (CNS). Therefore, the authors examined the effect of electromagnetic fields emitted by cellular phones (CPEMFs) on the evoked neuronal activity of CNS relating to generation and representation of electrodermal activity (EDA), an index of sympathetic nervous system activity. EDA (skin resistance response; SRR) latency was lengthened approximately 200 ms with CPEMFs exposure irrespective of the head site next to mobile phone used. Hemispheric asymmetry of EDA-2 pathway, which is represented by shorter SRR latency in the right hand of the right hand responders, was also distorted with CPEMFs. Because the CNS regions including EDA-2 are also involved in tasks of motor timing and time estimation, delayed response in this neuronal network due to CPEMFs exposure may increase the response time of mobile phone users. <u>Therefore, the findings point to the potential risks</u> of mobile phones on the function of CNS and consequently, possible increase in the risk <u>of phone-related driving hazards.</u>

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

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: <u>The modulation of the expression of Hsps in neuronal cells can</u> <u>be an early response to radiofrequency microwaves.</u>

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

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.

### **Hearing Effects**

## Panda NK, Modi R, Munjal S, Virk RS. Auditory changes in mobile users: is evidence forthcoming?<u>Otolaryngol Head Neck Surg.</u> 144(4):581-585, 2011.

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. <u>CONCLUSION:Long-term</u> <u>and intensive GSM and CDMA mobile phone use may cause damage to cochlea as well as the</u> <u>auditory cortex.</u>

## 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.

Abstract. 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, crosssectional, 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. Highfrequency 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.

## <u>Oktay MF</u>, <u>Dasdag S</u>. Effects of intensive and moderate cellular phone use on hearing function. <u>Electromagn Biol Med.</u> 25(1):13-21, 2006.

The purpose of this study is to investigate the effects of radiation emitted by mobile phones on the hearing of users. The study was carried out on three groups: 1) 20 men who have used a cellular phone frequently and spoken approximately 2 h per day for four years; 2) 20 men who have used a cellular phone for 10-20 min per day for four

years; and 3) 20 healthy men who have never used a cellular phone (the control group). Brainstem evoked response audiometric (BERA) and pure tone audiometric (PTA) methods were used to measure the effects of exposure on hearing function of the subjects. In BERA measurements, I-III, III-V, and I-V interpeak latencies were evaluated. Interpeak latency of subjects in two experimental groups was compared to that of subjects in the control group. The BERA results showed no differences among the groups (p > 0.05).In PTA measurements, detection thresholds at 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, and 8000 Hz frequencies were measured in all three groups. No differences were observed between moderate mobile phone users (10-20 min. per day) and control subjects. However, detection thresholds in those who talked approximately 2 h per day were found to be higher than those in either moderate users or control subjects. Differences at 4000 Hz for both bone and air conduction for right ears, and 500 Hz, and 4000 Hz bone and air conduction for left ears were significant for mean hearing threshold. This study shows that a higher degree of hearing loss is associated with longterm exposure to electromagnetic (EM) field generated by cellular phones.

# <u>Meo SA</u>, <u>Al-Drees AM</u>. Mobile phone related-hazards and subjective hearing and vision symptoms in the Saudi population. Int J Occup Med Environ Health. 18(1):53-57, 2005

OBJECTIVES: Over the past decade utilization of mobile phones has dramatically increased. They are now an essential part of business, commerce, and communication, however, their use may lead to health problems. Therefore, the present study was designed to investigate a link between the use of mobile phones and hearing and vision symptoms in the Saudi population and also to contribute to the increase in social awareness of health problems associated with the use of these devices. MATERIALS AND METHODS: A total of 873 (57.04% of males and 39.86% of females) subjects using mobile phones were invited to participate in the presented study. A structured questionnaire was distributed among them to collect a detailed medical history. The Chi-square test was employed to observe the relationship between duration of calls and hearing and vision complaints. RESULTS: The present study showed an association between the use of mobile phones and hearing and vision complaints. About 34.59% of problems were related with impaired hearing, ear ache and/or warmth on the ear, and 5.04% of complaints with the decreased and/or blurred vision. CONCLUSIONS: It is concluded that the use of mobile phone is a health risk factor, and thus it is suggested that excessive use of mobile phones should be avoided and social awareness increased through health promotion activities, such as group discussions or public presentations and via electronic and printed media sources.

### 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.

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). <u>Chronic usage mobile phone revealed high frequency hearing loss in the dominant ear (mobile phone used) compared to the non-dominant ear.</u>

### 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. 2014 May 1:1-6. [Epub ahead of print]

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.

Kerekhanjanarong V, Supiyaphun P, Naratricoon J, Laungpitackchumpon P. The effect of mobile phone to audiologic system. J Med Assoc Thai. 88 Suppl 4:S231-234, 2005. Mobile phones have come into widespread use. There are a lot of possible adverse effect to health. Use of mobile phone generate potentially harmful radiofrequency electromagnetic field (EMF) particularly for the hearing aspect. 98 subjects underwent hearing evaluations at Department of Otolaryngology, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University. 31 males and 67females, mean age was 30.48 +/- 9.51 years old, all subjects were investigated the hearing level by audiometry, tympanometry, otoacoustic emission (OAE) and auditory brain stem evoked response (ABR). The average of using time were 32.54 +/- 27.64 months, 57 subjects usually used the right side and 41 the left side. Average time of use per day was 26.31 +/- 30.91 minutes (range from 3 to 180 mins). When the authors compared the

audiogram, both pure tone and speech audiometry, between the dominant and nondominant side, it indicated that there is no significant different. When the authors focused on the 8 subjects that used the mobile phone more than 60 mins per day. It indicated that the hearing threshold of the dominant ears was worse than the nondominant ears.

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. 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.

Kellenyi, L, Thuroczy, G, Faludy, B, Lenard, L, Effects of mobile GSM radiotelephone exposure on the auditory brainstem response (ABR). Neurobiology 7:79-81, 1999. A 15-min exposure to GSM phone radiation caused an increase in auditory brainstem response in the exposed side of human subjects. Subjects also showed a hearing deficiency in the high frequency range (20 dB hearing deficiency from 2 KHz to 10 KHz).

## 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.

Abstract. 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.

### Hutter HP, Moshammer H, Wallner P, Cartellieri M, Denk-Linnert DM, Katzinger M, Ehrenberger K, Kundi M. Tinnitus and mobile phone use. Occup Environ Med. 67(12):804-808, 2010.

Objectives The mechanisms that produce tinnitus are not fully understood. While tinnitus can be associated with diseases and disorders of the ear, retrocochlear diseases and vascular pathologies, there are few known risk factors for tinnitus apart from these conditions. There is anecdotal evidence of an link between mobile phone use and tinnitus, but so far there have been no systematic investigations into this possible association. Methods 100 consecutive patients presenting with tinnitus were enrolled in an individually matched case-control study. For each case a control subject was randomly selected from visiting outpatients matched for sex and age. The patient's history was obtained and clinical examinations were conducted to exclude patients with known underlying causes of tinnitus. Mobile phone use was assessed based on the Interphone Study protocol. ORs were computed by conditional logistic regression with years of education and living in an urban area as covariates. Results Mobile phone use up to the index date (onset of tinnitus) on the same side as the tinnitus did not have significantly elevated ORs for regular use and intensity or for cumulative hours of use. The risk estimate was significantly elevated for prolonged use (>/=4 years) of a mobile phone (OR 1.95; CI 1.00 to 3.80). Conclusions Mobile phone use should be included in future investigations as a potential risk factor for developing tinnitus.

## Cox RA, Luxton LM, Cerebral symptoms from mobile telephones. *Occup Environ Med* 57(6):431, 2000. (letter to the editor)

Mobile phones affect the inner ear in 5-8% of users leading to dizziness, disorientation, nausea, headache and transient confusion.

# Alsanosi AA, Al-Momani MO, Hagr AA, Almomani FM, Shami IM, Al-Habeeb SF. The acute auditory effects of exposure for 60 minutes to mobile`s electromagnetic field. Saudi Med J. 34(2):142-146, 2013.

**OBJECTIVE:** To assess the immediate consequences of 60 minutes exposure to mobile phones on hearing function by determining changes in distortion product otoacoustic emission (DPOAE) and hearing threshold levels (HTLs). **METHODS:** This prospective

control clinical trial study was carried out at the Ear, Nose and Throat Department, King Abdulaziz University Hospital, Riyadh, Kingdom of Saudi Arabia from July 2009 to July 2011. The data collected included age, symptoms experienced after exposure, and HTLs and DPOAE were recorded before, and immediately after 60 minutes of exposure to the same model of mobile phone. **RESULTS:** Heat/pain was the most commonly reported symptom. In the test-ears, significant shift (p<0.05) was noticed in HTLs at 1000 and 2000 Hz but not at other frequencies, while non test-ears did not reveal significant shift in HTLs. Additionally, test-ears revealed significant differences (p<0.05) in DPOAE at 1000 Hz, 1400 Hz, 2000 Hz, and at the average of all frequencies, while non test-ears did not show significant differences. **CONCLUSION:** Sixty minutes of close exposure to electromagnetic fields emitted by a mobile phone had an immediate effect on HTL assessed by pure-tone audiogram and inner ear (assessed by DPOAE) in young human subjects. It also caused a number of other otologic symptoms.

### 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. 2013 Apr 25. doi: 10.1002/lary.24103. [Epub ahead of print]

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.

## Grisanti G, Parlapiano C, Tamburello CC, Tine G, Zanforlin L. Cellular phone effects on otoacoustic emissions. IEEE MTT-S Digest 2: 771-774, 1998.

A study on bioelectromagnetic effects induced by the use of TACS phones, evidencing a variation of the natural response of the auditory system is presented. This study was performed applying a method based on the registration of the evoked otoacosutic

emissions (transient and distortion products). <u>The experimental results show that</u> <u>modulated electromagnetic fields modify the distortion products in about all the</u> <u>examined subjects.</u>

Garcia Callejo FJ, Garcia Callejo F, Pena Santamaria J, Alonso Castaneira I, Sebastian Gil E, Marco Algarra J. [Hearing level and intensive use of mobile phones] Acta Otorrinolaringol Esp. 56(5):187-191, 2005. [Article in Spanish] INTRODUCTION: Wide studies and substantial controversies build on utilization of actual mobile phones and appearance of systemic disorders or even tumours, but there is no knowledge about an eventual involvement on early hearing loss. PATIENTS AND METHODS: In a group of three hundred and twenty-three healthy and normoacoustic volunteers who were usual costumers of mobile phones an audiometric evaluation was made at the beginnig of its use and three years later, inquiring about the periods of time per day and year employed on direct contacts with phone. A healthy and normoacoustic control group of non users was studied too. RESULTS: Cases carried out 24.3 +/- 8.2 active contacts, reaching 50.4 +/- 27.8 days of mobile phone employment in three years. Audiometric curve was similar in cases and controls at the beginning of the study. After this follow-up, cases showed an increase on hearing threshold between 1 and 5 dB HL more than controls in speech tones (p<0.001). Moreover, there was a trend to correlate time of phone use to hearing impairment, but this finding did not result statistically significative. CONCLUSIONS: Frequent management of mobile phones in a middle period of time allows to detect a mild hearing loss, but the cause of this disorder keeps unclear.

# Fritze K, Wiessner C, Kuster N, Sommer C, Gass P, Hermann DM, Kiessling M,Hossmann KA, Effect of global system for mobile communication microwave exposure on the genomic response of the rat brain. Neuroscience 81(3):627-639, 1997.

The acute effect of global system for mobile communication (GSM) microwave exposure on the genomic response of the central nervous system was studied in rats by measuring changes in the messenger RNAs of hsp70, the transcription factor genes c-fos and c-jun and the glial structural gene GFAP using in situ hybridization histochemistry. Protein products of transcription factors, stress proteins and marker proteins of astroglial and microglial activation were assessed by immunocytochemistry. Cell proliferation was evaluated by bromodeoxyuridine incorporation. A special GSM radiofrequency test set, connected to a commercial cellular phone operating in the discontinuous transmission mode, was used to simulate GSM exposure. The study was conducted at time averaged and brain averaged specific absorption rates of 0.3 W/kg (GSM exposure), 1.5 W/kg (GSM exposure) and 7.5 W/kg (continuous wave exposure), respectively. Immediately after exposure, in situ hybridization revealed slight induction of hsp70 messenger RNA in the cerebellum and hippocampus after 7.5 W/kg exposure, but not at lower intensities. A slightly increased expression of c-fos messenger RNA was observed in the cerebellum, neocortex and piriform cortex of all groups subjected to immobilization, but no differences were found amongst different exposure conditions. C-jun and GFAP messenger RNAs did not increase in any of the experimental groups. 24 h after exposure, immunocytochemical analysis of FOS and JUN proteins (c-FOS, FOS B,

c-JUN JUN B, JUN D), of HSP70 or of KROX-20 and -24 did not reveal any alterations. Seven days after exposure, neither increased cell proliferation nor altered expression of astroglial and microglial marker proteins were observed. <u>In conclusion, acute high</u> <u>intensity microwave exposure of immobilized rats may induce some minor stress</u> <u>response</u> but does not result in lasting adaptive or reactive changes of the brain.

## <u>Colletti V, Mandalà M, Manganotti P, Ramat S, Sacchetto L, Colletti L</u>. Intraoperative observation of changes in cochlear nerve action potentials during exposure to electromagnetic fields generated by mobile phones. <u>J Neurol Neurosurg</u> Psychiatry.82(7):766-71, 2010

Background The rapid spread of devices generating electromagnetic fields (EMF) has raised concerns as to the possible effects of this technology on humans. The auditory system is the neural organ most frequently and directly exposed to electromagnetic activity owing to the daily use of mobile phones. In recent publications, a possible correlation between mobile phone usage and central nervous system tumours has been detected. Very recently a deterioration in otoacoustic emissions and in the auditory middle latency responses after intensive and long-term magnetic field exposure in humans has been demonstrated. Methods To determine with objective observations if exposure to mobile phone EMF affects acoustically evoked cochlear nerve compound action potentials, seven patients suffering from Ménière's disease and undergoing retrosigmoid vestibular neurectomy were exposed to the effects of mobile phone placed over the craniotomy for 5 min. Results All patients showed a substantial decrease in amplitude and a significant increase in latency of cochlear nerve compound action potentials during the 5 min of exposure to EMF. These changes lasted for a period of around 5 min after exposure. Discussion The possibility that EMF can produce relatively long-lasting effects on cochlear nerve conduction is discussed and analysed in light of contrasting previous literature obtained under non-surgical conditions. Limitations of this novel approach, including the effects of the anaesthetics, craniotomy and surgical procedure, are presented in detail.

# **Budak GG**, <u>Muluk NB</u>, <u>Budak B</u>, <u>Oztürk GG</u>, <u>Apan A</u>, <u>Seyhan N</u>. Effects of intrauterine and extrauterine exposure to GSM-like radiofrequency on distortion product otoacoustic emissions in infant male rabbits. <u>Int J Pediatr Otorhinolaryngol.</u> 73(3):391-399, 2009.

OBJECTIVES: The aim of this study was to investigate the potential hazardous effects of intrauterine (IU) and/or extrauterine (EU) exposure to 1800 MHz Global System for Mobile Communications-like (GSM-like) radiofrequency (RF) on the cochlear functions of infant rabbits by measuring distortion product otoacoustic emission (DPOAE) response amplitudes. METHODS: Thirty-six white infant male New Zealand rabbits each 1-month-old were included in the study. The animals were randomly divided into four groups. Nine infant rabbits (Group 1) were not exposed to 1800 MHz GSM-like RF (Control-C). Nine infant rabbits (Group 2) were exposed to 1800 MHz GSM-like RF, 15 min daily for 14 days after they reached 1-month of age (extrauterine-EU). Nine infant rabbits (Group 3) were exposed to 1800 MHz GSM-like RF, 15 min daily for 7 days in the

intrauterine period (between 15th and 22nd days of the gestational period) (intrauterine-IU). Nine infant rabbits (Group 4) were exposed to 1800 MHz GSM-like RF, 15 min daily for 7 days in the intrauterine period (between 15th and 22nd days of the gestational period) and 15 min daily for 14 days after they reached to 1-month of age (IU+EU). The cochlear functions were assessed by DPOAEs at 1.0-8.0 kHz. RESULTS: At 1.5 kHz, the mean DPOAE amplitude of Group 3 was higher than that of the controls and Group 2; and the mean DPOAE value of Group 4 was higher than that of the controls and Group 2. At 2.0 kHz, the mean DPOAE amplitude of Group 4 was higher than that of Group 2. At 3.0 kHz, the mean DPOAE amplitude of Group 4 was higher than that of the controls and Group 2. At 4.0 kHz, the mean DPOAE amplitude of Group 2 was lower than that of the controls, while the mean value of Group 4 was higher than the mean value of the controls and Group 2. At 6.0 kHz, the mean DPOAE amplitude of Group 2 was lower than that of the control group; however, the mean value of Group 4 was higher than that of Group 2. At 1.0 and 8.0 kHz, no significant differences were found among the four groups. CONCLUSION: Prolonged exposure and hyperthermia related to the power density of applied RF, increasing the temperature in the ear canal, may affect DPOAE amplitudes. Harmful effects of RF are mainly observed as a decrease in DPOAE amplitudes at 4.0-6.0 kHz during extrauterine exposure in infancy. During the intrauterine period, the water content of the middle and inner ear and amnion fluid may play a protective role. Therefore, children must be protected from RF exposure. The use of mobile phones at short distances from the ear of the infants should be avoided because of the lower thickness of the anatomical structure in infancy.

### Tahvanainen K, Nino J, Halonen P, Kuusela T, Alanko T, Laitinen T, Lansimies E, Hietanen M, Lindholm H. Effects of cellular phone use on ear canal temperature measured by NTC thermistors. Clin Physiol Funct Imaging. 27(3):162-172, 2007. The earlier studies using phantom models and human subjects concerning warming effects during cellular phone use have been controversial, partly because radiofrequency (RF) exposures have been variable. In this randomized, double-blind, placebo-controlled crossover trial, 30 healthy subjects were submitted to 900 MHz (2W) and 1800 MHz (1W) cellular phone RF exposure, and to sham exposure in separate study sessions. Temperature signals were recorded continuously in both ear canals before, during and after the 35-min RF exposure and the 35-min sham exposure sessions. Temperature was measured by using small-sized NTC thermistors placed in the ear canals through disposable ear plugs. The mean temperature changes were determined during a set cardiovascular autonomic function studies: during a 5-min controlled breathing test, during a 5-min spontaneous breathing test, during 7-min head-up tilting, 1-min before, during and after two consecutive Valsalva manoeuvres and during a deep breathing test. Temperatures in the exposed ear were significantly higher during RF exposures compared with sham exposure in both 900 and 1800 MHz studies with maximum differences of 1.2 +/- 0.5 degrees C (900 MHz exposure) and 1.3 +/- 0.7 degrees C (1800 MHz exposure). Temperatures in the RF-exposed ear were also significantly higher during the postexposure period compared with post-sham exposure period with maximum differences of 0.6 +/- 0.3 degrees C for 900 MHz and 0.5 +/- 0.5

degrees C for 1800 MHz. <u>The results of this study suggest that RF exposure to a cellular</u> phone, either using 900 or 1800 MHz with their maximal allowed antenna powers, <u>increases the temperature in the ear canal.</u> The reason for the ear canal temperature rising is a consequence of mobile phone battery warming during maximal antenna power use. The earlier published articles do not indicate that temperature rising in the ear canal has any significant contribution from the RF fields emitted from mobile phones.

### Budak GG, Muluk NB, Budak B, Oztürk GG, Apan A, Seyhan N. Effects of GSM-like radiofrequency on distortion product otoacoustic emissions of rabbits: comparison of infants versus adults. Int J Pediatr Otorhinolaryngol. 73(8):1143-1147, 2009. OBJECTIVES: The aim of this study is to investigate the potential hazardous effects of 1800 MHz Global System for Mobile Communications-like (GSM-like) Radiofrequency (RF) exposure on the cochlear functions of female infant and adult rabbits by measuring Distortion Product Otoacoustic Emission (DPOAE) response amplitudes. METHODS: Eighteen each one-month-old New Zealand White female rabbits and eighteen each 13month-old adult rabbits were included into the study. They were randomly divided into four groups. Nine infant rabbits (Group 1) were not exposed to 1800 MHz GSM-like RF (Infant Control, C-In). Nine infant rabbits (Group 2) were exposed to 1800 MHz GSM-like RF, 15 min daily for 7 days after they reached one-month of age (Infant RF, RF-In). Nine adult rabbits were not exposed to 1800 MHz GSM-like RF, 15 min daily for 7 (Adult Control, C-Ad). Nine adult rabbits were exposed to 1800 MHz GSM-like RF, 15 min daily for 7 days (Adult RF, RF-Ad). Cochlear functions were assessed by DPOAEs at 1.0-8.0 kHz. RESULTS: At 1.0-2.0 and 6.0 kHz, the mean DPOAE values of Group 2 were significantly higher than that of Group 1. At 3.0-8.0 kHz, the mean DPOAE values of Group 4 were significantly lower than that of Group 1. At 6.0-8.0 kHz, the mean DPOAE values of Group 2 were significantly higher than that of Group 3. At 1.0-8.0 kHz, the mean DPOAE values of Group 4 were significantly lower than that of Group 2. At 1.0-8.0 kHz, the mean DPOAE values of Group 4 were significantly lower than that of Group 3. CONCLUSION: Harmful effects of GSM-like 1800 MHz RF exposure was detected more in the adult female rabbits than infant female rabbits by DPOAE measurement. Prolonged exposure and hyperthermia related to the power density of applied RFR, increasing the temperature in the ear canal, may decrease the DPOAE amplitudes. Water containing medium in the middle ear of infant rabbits may play the protective role from the RF damage.

#### <u>Budak GG</u>, <u>Muluk NB</u>, <u>Oztürk GG</u>, <u>Budak B</u>, <u>Apan A</u>, <u>Seyhan N</u>, <u>Sanli C</u>. Effects of GSMlike radiofrequency on distortion product otoacoustic emissions in pregnant adult rabbits. <u>Clin Invest Med.</u> 32(2):E112-116, 2009.

OBJECTIVES: To determine the effects of 1800 MHz GSM-like Radiofrequency (RFR) on the cochlear functions of pregnant adult rabbits by Distortion Product Otoacoustic Emissions (DPOAEs). METHODS: Eighteen 13-month-old pregnant and eighteen 13month-old non-pregnant New Zealand White rabbits were studied. They were randomly divided into four groups. Nine pregnant rabbits (Group 2) and nine non-pregnant rabbits

(Group 4) were exposed to 1800 MHz GSM-like RFR 15 min daily for 7 days. Nine pregnant (Group 1) and nine non-pregnant rabbits (Group 3) were not exposed to GSM like RFR. Cochlear functions were assessed by DPOAEs at 1.0-8.0 kHz. RESULTS: In all pregnant groups except 2.0 kHz, DPOAE amplitudes were not different in Group 2 and Group1. In Group 4, DPOAE amplitudes at 1.0-4.0 kHz (-1.68 dB SPL at 1.0 kHz, 3.05 dB SPL at 1.5 kHz, 2.96 dB SPL at 2.0 kHz, 1.30 dB SPL at 3.0 kHz and 12.22 dB SPL at 4.0 kHz) were lower than Group 3 (8.67 dB SPL at 1.0 kHz, 17.67 dB SPL at 1.5 kHz, 26.10 dB SPL at 2.0 kHz, 18.10 dB SPL at 3.0 kHz and 35.13 dB SPL at 4.0 kHz) (P < 0.0125). In the pregnant group, harmful effects of GSM-like RFR were less than in the non-pregnant group. CONCLUSION: <u>GSM-like RFR caused decreases in DPOAE amplitudes mainly in non-pregnant adult rabbits. Prolonged exposure may affect the DPOAE amplitude.</u> Recommendations are given to prevent the potential hazardous effects of RF in humans.

## <u>Al-Dousary SH</u> Mobile phone induced sensorineural hearing loss. <u>Saudi Med J.</u> 28(8):1283-1286, 2007.

The increased use of mobile phones worldwide has focused interest on the biological effects and possible health outcomes of exposure to radiofrequency fields from mobile phones, and their base stations. Various reports suggest that mobile phone use can cause health problems like fatigue, headache, dizziness, tension, and sleep disturbances; however, only limited research data is available in medical literature regarding interaction between electromagnetic fields emitted by mobile phones and auditory function; and the possible impact on hearing. We report a case of sensorineural hearing loss due to Global System for Mobile Communications mobile phone use, in a 42-year-old male.

### **Effects on Eyes**

#### Yu Y, <u>Yao K</u>. Non-thermal cellular effects of lowpower microwave radiation on the lens and lens epithelial cells. <u>J Int Med Res.</u> 38(3):729-736, 2010.

Because of the increased use of modern radiofrequency devices, public concern about the possible health effects of exposure to microwave radiation has arisen in many countries. It is well established that high-power microwave radiation can induce cataracts via its thermal effects. It remains unclear whether low-power microwave radiation, especially at levels below the current exposure limits, is cataractogenic. This review summarizes studies on the biological effects of low-power microwave radiation on lens and lens epithelial cells (LECs). It has been reported that exposure affects lens transparency, alters cell proliferation and apoptosis, inhibits gap junctional intercellular communication, and induces genetic instability and stress responses in LECs. These results raise the question of whether the ambient microwave environment can induce non-thermal effects in the lens and whether such effects have potential health consequences. Further in vivo studies on the effects on the lens of exposure to low-power microwave radiation are needed.

# Balik HH, Turgut-Balik D, Balikci K, Ozcan IC. Some ocular symptoms and sensations experienced by long term users of mobile phones. Pathol Biol (Paris). 53(2):88-91, 2005.

In this study, a survey was conducted to investigate the possible effects of long term usage of mobile phone (MP) on eyes. The studied symptoms are blurring of vision, redness on the

, vision disturbance, secretion of the eyes, inflammation in the eyes and lacrimation of the eyes. There is no effect on redness on the eyes and vision disturbance, but some <u>statistical evidences are found that MP may cause blurring of vision, secretion of the</u> <u>eyes, inflammation in the eyes and lacrimation of the eyes.</u> These results suggest an awareness of the symptoms and sensations.

#### Yu Y, Yao K, Wu W, Wang K, Chen G, Lu D. Effects of exposure to 1.8 GHz

## radiofrequency field on the expression of Hsps and phosphorylation of MAPKs in human lens epithelial cells. <u>Cell Res.</u> 18(12):1233-1235, 2008.

(No abstract available) Last sentence of discussion:

"Our results suggest that exposure to RF of wireless communications can induce expression of Hsp27 and Hsp70 and the activation of ERK1/2 and JNK1/2 in human LECs. The induction of Hsp27 and Hsp70, by a non-thermal stress, together with the activation of signal transduction pathways, provides reliable and sensitive biomarkers that could serve as the basis for improved mobile phone safety guidelines."

#### Dovrat A, Berenson R, Bormusov E, Lahav A, Lustman T, Sharon N, Schachter L. Localized effects of microwave radiation on the intact eye lens in culture conditions. Bioelectromagnetics. 26(5):398-405, 2005.

A novel experimental system was used to investigate the localized effects of microwave radiation on bovine eye lenses in culture for over 2 weeks. <u>Using this setup, we found clear evidence that this radiation has a significant impact on the eye lens. At the macroscopic level, it is demonstrated that exposure to a few mW at 1 GHz for over 36 h affects the optical function of the lens. Most importantly, self-recovery occurs if the exposure is interrupted. At the microscopic level, close examination of the lens indicates that the interaction mechanism is completely different from the mechanism-causing cataract via temperature increase. Contrary to the latter's effect, that is particularly pronounced in the vicinity of the sutures and it is assumed to be a result of local friction between the edges of the fibers consisting the lens. Even if macroscopically the lens has recovered from the irradiation, microscopically the indicators of radiation impact remain.</u>

# Lu L, Xu H, Wang X, Guo G.Increased nitric oxide synthase activity is essential for electromagnetic-pulse-induced blood-retinal barrier breakdown in vivo.Brain Res. 1264:104-10, 2009.

**PURPOSE:** To examine whether electromagnetic pulses (EMPs) affected the permeability of the blood-retinal barrier (BRB), gene expression of occludin and activity

of nitric oxide synthase (NOS).**METHODS:** Sprague-Dawley (SD) rats were used and randomized into EMP and control groups. Retinas were removed immediately, and 2 h or 24 h after EMP radiation. BRB permeability was analyzed by transmission electron microscopy and Evans Blue staining. Retinal NOS activity and concentrations of nitrite and nitrate were measured. Occludin mRNA and protein levels were detected by RT-PCR and Western blotting. **RESULTS:** Exposure of SD rats to EMP resulted in increased BRB permeability, with the greatest decrease in occludin at 24 h. Moreover, this permeability defect was also correlated with significant increases in the formation of NO and induction of NOS activity in SD rats. Furthermore, we found that treatment with NOS inhibitor N-nitro-L-arginine methyl ester (L-NAME) blocked BRB breakdown and prevented the increase in NO formation and induction of NOS activity, as well as the decrease in occluding expression.**CONCLUSION:** Taken together, these results support the view that NOS-dependent NO production is an important factor that contributes to EMP-induced BRB dysfunction, and suggests that NOS induction may play an important role in BRB breakdown.

#### Teerapot Wessapan, Phadungsak Rattanadecho. Specific absorption rate and temperature increase in the human eye due to electromagnetic fields exposure at different frequencies. International Journal of Heat and Mass Transfer, 64:426-435, September 2013.

This study presents a numerical analysis of the specific absorption rate (SAR) and the heat transfer in a heterogeneous human eye model exposed to electromagnetic (EM) fields of 900 and 1800 MHz. In this study, the effect of operating frequency on the SAR and temperature distributions in the eye was systematically investigated. The SAR value and the temperature distribution in various tissues in the eye during exposure to EM fields were obtained by numerical simulation of EM wave propagation and a heat transfer model was then developed based on the natural convection and porous media theories. The study highlights two transport phenomena: heat and mass transfer in the eye during exposure to EM fields at different frequencies. This study indicated that when the eye exposed to EM fields at the frequencies of 900 and 1800 MHz, the highest SAR values at two chosen frequencies was in the cornea, and the highest temperature at the frequency of 900 MHz was in the anterior chamber while the highest for the frequency of 1800 MHz was in the vitreous. The temperature distribution in the eye induced by EM fields was not directly related to the SAR distribution due to the effect of the interaction among the dielectric properties, thermal properties, blood perfusion, and penetration depth of the EM power. Moreover, this study also showed that the exposure time had an influence on the temperature increase in the eye.

## Teerapot Wessapan, Phadungsak Rattanadecho. Influence of ambient temperature on heat transfer in the human eye during exposure to electromagnetic fields at 900 MHz. International Journal of Heat and Mass Transfer 70: 378-388, 2014.

The topic of temperature increase in human tissue when exposed to EM fields, particularly those radiated to the eye, has been of interest for many years. This study

presents a numerical analysis of the specific absorption rate (SAR) and the heat transfer in a heterogeneous two-dimensional human eye model exposed to TM-mode of electromagnetic (EM) fields of 900 MHz at various power densities. In this study, the effects of ambient temperature and power density on the temperature distributions and fluid flow in the eye during exposure to electromagnetic fields were systematically investigated. The electric field, SAR, temperature distribution and fluid flow in various tissues in the eye during exposure to EM fields were obtained by numerical simulation of EM wave propagation and a heat transfer model. The heat transfer model was then developed based on the porous media theories. The study highlights heat transfer and fluid flow in the eye during exposure to EM fields at different ambient temperatures. This study indicated that when the eye exposed to EM fields at the frequency of 900 MHz, the highest electric field intensity and SAR values at the chosen frequency was in the cornea. At the highest power density of 100 mW/cm<sup>2</sup>, the absorbed EM energy is converted to heat causes a further increase of 3 °C in corneal temperature in cases of hot, moderate and cold ambient temperatures. The result shows important information related to a complex interaction between ambient temperature, fluid flow and temperature distribution in the eye during exposure to electromagnetic fields. Moreover, this study also showed that the power density had a strong influence on the temperature increase and fluid flow in the eye.

## **Balci M**, **Devrim E**, **Durak I**. Effects of mobile phones on oxidant/antioxidant balance in cornea and lens of rats. **Curr Eye Res.** 32(1):21-25, 2007.

Purpose: To investigate the effects of mobile-phone-emitted radiation on the oxidant/antioxidant balance in corneal and lens tissues and to observe any protective effects of vitamin C in this setting. Methods: Forty female albino Wistar rats were assigned to one of four groups containing 10 rats each. One group received a standardized daily dose of mobile phone radiation for 4 weeks. The second group received this same treatment along with a daily oral dose of vitamin C (250 mg/kg). The third group received this dose of vitamin C alone, while the fourth group received standard laboratory care and served as a control. In corneal and lens tissues, malondialdehyde (MDA) levels and activities of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT) were measured with spectrophotometric methods. Results: In corneal tissue, MDA level and CAT activity significantly increased in the mobile phone group compared with the mobile phone plus vitamin C group and the control group (p < 0.05), whereas SOD activity was significantly decreased (p < 0.05). In the lens tissues, only the MDA level significantly increased in the mobile phone group relative to mobile phone plus vitamin C group and the control groups (p < 0.05). In lens tissue, significant differences were not found between the groups in terms of SOD, GSH-Px, or CAT (p > 0.05). Conclusions: The results of this study suggest that mobile telephone radiation leads to oxidative stress in corneal and lens tissues and that antioxidants such as vitamin C can help to prevent these effects

## <u>Lixia S, Yao K, Kaijun W, Deqiang L, Huajun H, Xiangwei G, Baohong W, Wei Z, Jianling L, Wei W</u>. Effects of 1.8GHz radiofrequency field on DNA damage and expression of

heat shock protein 70 in human lens epithelial cells. <u>Mutat Res.</u>602(1-2):135-142, 2006.

To investigate the DNA damage, expression of heat shock protein 70 (Hsp70) and cell proliferation of human lens epithelial cells (hLEC) after exposure to the 1.8GHz radiofrequency field (RF) of a global system for mobile communications (GSM). An Xc-1800 RF exposure system was used to employ a GSM signal at 1.8GHz (217Hz amplitudemodulated) with the output power in the specific absorption rate (SAR) of 1, 2 and 3W/kg. After 2h exposure to RF, the DNA damage of hLEC was accessed by comet assay at five different incubation times: 0, 30, 60, 120 and 240min, respectively. Western blot and RT-PCR were used to determine the expression of Hsp70 in hLECs after RF exposure. The proliferation rate of cells was evaluated by bromodeoxyuridine incorporation on days 0, 1 and 4 after exposure. The results show that the difference of DNA-breaks between the exposed and sham-exposed (control) groups induced by 1 and 2W/kg irradiation were not significant at any incubation time point (P>0.05). The DNA damage caused by 3W/kg irradiation was significantly increased at the times of 0 and 30min after exposure (P<0.05), a phenomenon that could not be seen at the time points of 60, 120 or 240min (P>0.05). Detectable mRNA as well as protein expression of Hsp70 was found in all groups. Exposure at SARs of 2 and 3W/kg for 2h exhibited significantly increased Hsp70 protein expression (P<0.05), while no change in Hsp70 mRNA expression could be found in any of the groups (P>0.05). No difference of the cell proliferation rate between the sham-exposed and exposed cells was found at any exposure dose tested (P>0.05). The results indicate that exposure to non-thermal dosages of RF for wireless communications can induce no or repairable DNA damage and the increased Hsp70 protein expression in hLECs occurred without change in the cell proliferation rate. The non-thermal stress response of Hsp70 protein increase to RF exposure might be involved in protecting hLEC from DNA damage and maintaining the cellular capacity for proliferation.

## Gasmelseed A. Electromagnetic energy absorption patterns in subjects with common visual disorders. Electromagn Biol Med. 30(3):136-145, 2011.

This article describes the analysis of electromagnetic energy absorption properties of models of the human eye with common visual disorders. The investigation addresses two types of visual disorders, namely hyperopia (or farsightedness) and myopia (or nearsightedness). Calculations were carried out using plane multilayered method with common wireless communication frequencies of 900, 1800, and 2450 MHz. The effect of wireless radiation on the eye is studied by calculation of the specific absorption rate (SAR) in three different eye models. The results of the simulations confirmed the anticipated and more complex relationship between absorption and structural variations of the eye at these frequencies.

Ozguner F, Bardak Y, Comlekci S. Protective effects of melatonin and caffeic acid phenethyl ester against retinal oxidative stress in long-term use of mobile phone: A comparative study. <u>Mol Cell Biochem.</u> 282(1-2):83-88, 2006.

There are numerous reports on the effects of electromagnetic radiation (EMR) in various cellular systems. Melatonin and caffeic acid phenethyl ester (CAPE), a component of honeybee propolis, were recently found to be potent free radical scavengers and antioxidants. Mechanisms of adverse effects of EMR indicate that reactive oxygen species may play a role in the biological effects of this radiation. The present study was carried out to compare the efficacy of the protective effects of melatonin and CAPE against retinal oxidative stress due to long-term exposure to 900 MHz EMR emitting mobile phones. Melatonin and CAPE were administered daily for 60 days to the rats prior to their EMR exposure during our study. Nitric oxide (NO, an oxidant product) levels and malondialdehyde (MDA, an index of lipid peroxidation), were used as markers of retinal oxidative stress in rats following to use of EMR. Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) activities were studied to evaluate the changes of antioxidant status in retinal tissue. Retinal levels of NO and MDA increased in EMR exposed rats while both melatonin and CAPE caused a significant reduction in the levels of NO and MDA. Likewise, retinal SOD, GSH-Px and CAT activities decreased in EMR exposed animals while melatonin and CAPE caused a significant increase in the activities of these antioxidant enzymes. Treatment of EMR exposed rats with melatonin or CAPE increased the activities of SOD, GSH-Px and CAT to higher levels than those of control rats. In conclusion, melatonin and CAPE reduce retinal oxidative stress after long-term exposure to 900 MHz emitting mobile phone. Nevertheless, there was no statistically significant difference between the efficacies of these two antioxidants against to EMR induced oxidative stress in rat retina. The difference was in only GSH-Px activity in rat retina. Melatonin stimulated the retinal GSH-Px activity more efficiently than CAPE did.

## Lu L, Xu H, Wang X, Guo G.Increased nitric oxide synthase activity is essential for electromagnetic-pulse-induced blood-retinal barrier breakdown in vivo.Brain Res. 1264:104-10, 2009.

PURPOSE: To examine whether electromagnetic pulses (EMPs) affected the permeability of the **blood-retinal barrier (BRB)**, gene expression of occludin and activity of nitric oxide synthase (NOS). METHODS: Sprague-Dawley (SD) rats were used and randomized into EMP and control groups. Retinas were removed immediately, and 2 h or 24 h after EMP radiation. BRB permeability was analyzed by transmission electron microscopy and Evans Blue staining. Retinal NOS activity and concentrations of nitrite and nitrate were measured. Occludin mRNA and protein levels were detected by RT-PCR and Western blotting. RESULTS: Exposure of SD rats to EMP resulted in increased BRB permeability, with the greatest decrease in occludin at 24 h. Moreover, this permeability defect was also correlated with significant increases in the formation of NO and induction of NOS activity in SD rats. Furthermore, we found that treatment with NOS inhibitor N-nitro-L-arginine methyl ester (L-NAME) blocked BRB breakdown and prevented the increase in NO formation and induction of NOS activity, as well as the decrease in occluding expression. **CONCLUSION:** Taken together, these results support the view that NOS-dependent NO production is an important factor that contributes to EMP-induced BRB dysfunction, and suggests that NOS induction may play an important

role in BRB breakdown.

# <u>Hässig M</u>, <u>Jud F</u>, <u>Naegeli H</u>, <u>Kupper J</u>, <u>Spiess B</u>. Prevalence of nuclear cataract in Swiss veal calves and its possible association with mobile telephone antenna base stations. <u>Schweiz Arch Tierheilkd.</u> 151(10):471-478, 2009.

The purpose of this study was to valuate the prevalence of nuclear cataract in veal calves and to elucidate a possible impact by mobile phone base stations (MPBS). For this experiment a cohort study was conducted. A follow-up of the geographical location of each dam and its calf from conception through the fetal period up to slaughter was performed. The first trimester of gestation (organogenesis) was particularly emphasized. The activities of selected protective antioxidants (superoxide dismutase, catalase, glutathione peroxidase [GPx]) were assessed in aqueous humor of the eye to evaluate the redox status. Of 253 calves, 79 (32 %) had various degrees of nuclear cataract, but only 9 (3.6 %) calves had severe nuclear cataract. Results demonstrate a relation between the location of veals calves with nuclear cataracts in the first trimester of gestation and the strength of antennas. The number of antennas within 100 to 199 meters was associated with oxidative stress and there was an association between oxidative stress and the distance to the nearest MPBS. Oxidative stress was increased in eyes with cataract (OR per kilometer: 0.80, confidence interval 95 % 0.62,0.93). It has not been shown that the antennas actually affected stress. Hosmer-Lemeshow statistics showed an accuracy of 100 % in negative cases with low radiation, and only 11.11 % accuracy in positive cases with high radiation. This reflects, that there are a lot of other possibilities for nuclear cataract beside MPBS. Further studies on the influence of electromagnetic fields during embryonic development animal or person at risk are indicated.

## <u>Hässig M</u>, <u>Jud F</u>, <u>Spiess B</u>. [Increased occurrence of nuclear cataract in the calf after erection of a mobile phone base station]. <u>Schweiz Arch Tierheilkd</u>. 154(2):82-86, **2012**.[Article in German]

We examined and monitored a dairy farm in which a large number of calves were born with nuclear cataracts after a mobile phone base station had been erected in the vicinity of the barn. Calves showed a 3.5 times higher risk for heavy cataract if born there compared to Swiss average. All usual causes such as infection or poisoning, common in Switzerland, could be excluded. The real cause of the increased incidence of cataracts remains unknown.

#### Jelodar G, Akbari A, Nazifi S. The prophylactic Effect of Vitamin C on Oxidative Stress Indexes in Rat Eyes Following Exposure to Radiofrequency Wave Generated by a BTS Antenna Model. Int J Radiat Biol. 89(2):128-131, 2013.

Purpose: This study was conducted to evaluate the effect of radiofrequency wave (RFW)-induced oxidative stress in the eye and the prophylactic effect of vitamin C on this organ by measuring the antioxidant enzymes activity including: glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT), and malondialdehyde (MDA). Materials and methods: Thirty-two adult male Sprague-Dawley rats were

randomly divided into four experimental groups and treated daily for 45 days as follows: control, vitamin C (L-ascorbic acid 200 mg/kg of body weight/day by gavage), test (exposed to 900 MHz RFW) and the treated group (received vitamin C in addition to exposure to RFW). At the end of the experiment all animals were killed, their eyes were removed and were used for measurement of antioxidant enzymes and MDA activity. <u>Results: The results indicate that exposure to RFW in the test group decreased</u> <u>antioxidant enzymes activity and increased MDA compared with the control groups</u> (P<0.05). In the treated group vitamin C improved antioxidant enzymes activity and <u>reduced MDA compared to the test group (P<0.05). Conclusions: It can be concluded</u> <u>that RFW causes oxidative stress in the eyes and vitamin C improves the antioxidant</u> <u>enzymes activity and decreases MDA.</u>

# Liu X, Shen H, Shi Y, Chen J, Chen Y, Ji A. The microarray study on the stress gene transcription profile in human retina pigment epithelial cells exposed to microwave radiation. Zhonghua Yu Fang Yi Xue Za Zhi 36(5):291-294, 2002.

OBJECTIVE: To study the difference in stress and apoptosis related genes transcription between hTERT-RPE1 cells exposed to simulated microwave radiation and the cells with heat water bath, and the effects of microwave on gene transcription in cultured human retina pigment epithelial cells. METHODS: cDNA microarray technique was used to detect the mRNA isolated from hTERT-RPE1 cells exposed to **2 450 MHz** simulated microwave radiation and with heat water bath, respectively. RESULTS: Among the 97 related aim genes, there were seven genes up-regulating its transcription, i.e., M31166 (2.52fold), L24123 (2.66fold), AF039704 (2.22fold), U67156 (2.07fold), AF040958 (2.13fold), NM-001423 (2.63fold) and NM-005346 (3.68fold). But, no notably downregulating gene in transcription was detected. <u>CONCLUSIONS: Microwave could induce up-regulating in multiple stress and apoptosis related genes transcription in cultured human retina pigment epithelial cells, hTERT-RPE1 cells. Microwave radiation has unique effect itself in addition to its heat effect.</u>

# Akar A, Karayiğit MO, Bolat D, Gültiken ME, Yarım M, Castellani G. Effects of low level electromagnetic field exposure at 2.45 GHz on rat cornea. Int J Radiat Biol. 2012 Dec 3. [Epub ahead of print]

Abstract Purpose: To investigate the effects of low level Electromagnetic Field (low level-EMF) exposure, as frequently encountered in daily life, on the yesmal rat cornea using histological and stereological method. Methods: Twenty-two adult male Wistar rats were randomly divided into two groups: study group (n=11) and control group (n=11). Rats in the study group were exposed to 2.45 GHz **Microwave (MW) radiation** (11.96±0.89V/m), 0.25 W/kg specific absorption rate (SAR) for 2 hours each day for 21 days. The corneal thickness and the anterior epithelium corneal thickness were measured using two different methods. Results: Using the histological method, the mean corneal thicknesses in the control and study group were 278.9±54.5  $\mu$ m, and 272.4±85.6  $\mu$ m, respectively. There was no statistically significant difference between the groups (p>0.05). The anterior corneal epithelium thickness was 28.1±4.9  $\mu$ m in the control group and 31.7±5.5  $\mu$ m in the study group. There were statistically differences

between the groups with regard to the thickness of anterior epithelium (p<0.05). In the measurement made by the stereological method, the percentage of the cornea occupied by anterior corneal epithelium was 15.94% in the control group and 17.9% in the study group. Despite the fact that there was a relation between increased anterior epithelial area (AEA) and radiation exposure, no statistically significant relationship in area fraction of each compartment was found between the control and study groups. <u>Conclusions: Results of this preliminary study show that exposure to MW radiation might cause alterations in the rat cornea.</u>

# Tök L, Nazıroğlu M, Doğan S, Kahya MC, Tök O. Effects of melatonin on Wi-Fi-induced oxidative stress in lens of rats. Indian J Ophthalmol. 62(1):12-15, 2014. doi: 10.4103/0301-4738.126166.

Introduction: Melatonin has been considered a potent antioxidant that detoxifies a variety of reactive oxygen species in many pathophysiological states of eye. The present study was designed to determine the effects of Wi-Fi exposure on the lens oxidant, antioxidant redox systems, as well as the possible protective effects of melatonin on the lens injury induced by electromagnetic radiation (EMR). Materials and Methods: Thirtytwo rats were used in the current study and they were randomly divided into four equal groups as follows: First and second groups were cage-control and sham-control rats. Rats in third group were exposed to Wi-Fi (2.45 GHz) for duration of 60 min/day for 30 days. As in the third group, the fourth group was treated with melatonin. The one-hour exposure to irradiation in second, third and fourth took place at noon each day. Results: Lipid peroxidation levels in the lens were slightly higher in third (Wi-Fi) group than in cage and sham control groups although their concentrations were significantly (P < 0.05) decreased by melatonin supplementation. Glutathione peroxidase (GSH-Px) activity was significantly (P < 0.05) lower in Wi-Fi group than in cage and sham control groups although GSH-Px (P < 0.01) and reduced glutathione (P < 0.05) values were significantly higher in Wi-Fi + melatonin group than in Wi-Fi group. Conclusions: There are poor oxidative toxic effects of one hour of Wi-Fi exposure on the lens in the animals. However, melatonin supplementation in the lens seems to have protective effects on the oxidant system by modulation of GSH-Px activity.

# Pologea-Moraru R, Kovacs E, Iliescu KR, Calota V, Sajin G. The effects of low level microwaves on the fluidity of photoreceptor cell membrane. Bioelectrochemistry 56(1-2):223-225, 2002.

Due to the extensive use of electromagnetic fields in everyday life, more information is required for the detection of mechanisms of interaction and the possible side effects of electromagnetic radiation on the structure and function of the organism.<u>In this paper</u>, we study the effects of low-power microwaves **(2.45 GHz)** on the membrane fluidity of rod photoreceptor cells. The retina is expected to be very sensitive to microwave irradiation due to the polar character of the photoreceptor cells [Biochim. Biophys. Acta 1273 (1995) 217] as well as to its high water content [Stud. Biophys. 81 (1981) 39].

#### Yang R, Chen J, Deng Z, Liu X, [Effect of vitamin E on morphological variation of retinal

## ganglion cells after microwave radiation]. *Wei Sheng Yan Jiu* 30(1):31-33, 2001. [Article in Chinese]

To determine the morphological variation in the primary cultured pig retinal ganglion cells induced by microwave and the protection of VE can supply some experiment foundation for study of effect of microwave and its protection. Retinal ganglion cells of pig were cultured in vitro and added VE of different concentration, Each group was taken after 30 mW/cm2 microwave intensity radiated for 1 h in shielded room by **2450 MHz** continuous wave physiotherapy machine. Immediately after radiation, the morphological variation of cells was observed by optics microscope and transmission electronic microscope. The result showed that a portion of cells congregated, with their axon disappeared after radiation. Mitochondria and endoplasmic reticulum are detected swelling by transmission electronic microscope. The results showed that A poptosis cells can be observed. Cells of VE added groups had not obvious changes with optics microscope, but could be found that mitochondria swelling lightly and integrate mitochondria cristae by transmission electronic microscope. <u>The results showed that</u> <u>microwave induced the morphological damage in primary cultured retinal ganglion cells, VE could reduced the damage of retina ganglion cells by microwave in some extent.</u>

Behrens T, Lynge E, Cree I, Sabroe S, Lutz JM, Afonso N, Eriksson M, Guénel P, Merletti F, Morales-Suarez-Varela M, Stengrevics A, Févotte J, Llopis-González A, Gorini G, Sharkova G, Hardell L, Ahrens W. Occupational exposure to electromagnetic fields and sex-differential risk of uveal melanoma. Occup Environ Med.67(11):751-759, 2010 Objectives The association between occupational exposure to electromagnetic fields (EMF) and the risk of uveal melanoma was investigated in a case-control study in nine European countries. Methods Incident cases of uveal melanoma and population as well as hospital controls were included and frequency matched by country, 5-year birth cohort and sex. Subjects were asked whether they had worked close to high-voltage electrical transmission installations, computer screens and various electrical machines, or in complex electrical environments. Measurements of two Scandinavian job-exposure matrices were applied to estimate lifelong cumulative EMF exposure. Unconditional logistic regression analyses, stratified by sex and eye colour were calculated, adjusting for several potential confounders. Results 293 patients with uveal melanoma and 3198 control subjects were interviewed. Women exposed to electrical transmission installations showed elevated risks (OR 5.81, 95% CI 1.72 to 19.66). Positive associations with exposure to control rooms were seen among men and women, but most risk increases were restricted to subjects with dark iris colour. Application of published EMF measurements revealed stronger risk increases among women compared to men. Again, elevated risks were restricted to subjects with dark eye colour. Conclusion Although based on a low prevalence of exposure to potential occupational sources of EMF, our data indicate that exposed dark-eyed women may be at particular risk for uveal melanoma.

## Yao K, Wang KJ, Sun ZH, Tan J, Xu W, Zhu LJ, Lu de Q. Low power microwave radiation inhibits the proliferation of rabbit lens epithelial cells by upregulating P27Kip1

#### expression. Mol Vis. 10:138-143, 2004.

PURPOSE: The goal of this study was to examine the effects of low power microwave radiation (<10 mW/cm2) on the proliferation of cultured rabbit lens epithelial cells (RLEC). METHODS: Cultured RLEC were exposed to continuous microwave radiation at a frequency of **2,450 MHz** and power densities of 0.10, 0.25, 0.50, 1.00, and 2.00 mW/cm2 for 8 h. Cell morphologic changes were observed under a phase-contrast microscope. Cell viability was measured using the MTT assay and cell cycle analysis was measured using flow cytometry. After exposure to 2.00 mW/cm2 microwave radiation for 4, 6, and 8 h, the expression of cell cycle-regulatory proteins, P21WAF1 and P27Kip1, was examined using western blot analysis. Finally, the levels of P21WAF1 and P27Kip1 mRNA were analyzed by reverse transcription-polymerase chain reaction (RT-PCR). RESULTS: After 8 h of radiation treatment, cells treated with 0.50, 1.00, and 2.00 mW/cm2 microwave radiation exhibited decreased cell viability, increased cell condensation and an inhibition of DNA synthesis. RLEC showed significant G0/G1 arrest. No obvious changes could be detected in the 0.10 and 0.25 mW/cm2 microwave treatment groups. Protein expression of P27Kip1 was markedly increased after microwave radiation. However, the mRNA levels were unchanged. On the other hand, there were no detectable differences in P21WAF1 protein expression and mRNA levels between microwave treatment and control groups. CONCLUSIONS: This study suggests that low power microwave radiation higher than 0.50 mW/cm2 can inhibit lens epithelial cell proliferation, and increase the expression of P27Kip1. These effects may account for the decline of lens epithelial proliferation after exposure to microwave radiation.

# Kues HA, Monahan JC, D'Anna SA, McLeod DS, Lutty GA, Koslov S, Increased sensitivity of the non-human primate eye to microwave radiation following ophthalmic drug pretreatment. *Bioelectromagnetics* 13(5):379-393, 1992.

Previous studies in our laboratory have established that pulsed microwaves at 2.45 GHz and 10 mW/cm2 are associated with production of corneal endothelial lesions and with disruption of the blood-aqueous barrier in the non-human primate eye. In the study reported here we examined ocular damage in monkeys (M. mulatta and M. fascicularis) following topical treatment with one of two ophthalmic drugs (timolol maleate and pilocarpine) that preceded exposure to pulsed microwaves. Anesthetized monkeys were sham exposed or exposed to pulsed, 2.45 GHz microwaves (10 microseconds, 100 pps) at average power densities of 0.2, 1, 5, 10, or 15 mW/cm2 4 h a day for 3 consecutive days (respective SARs were 0.052, 0.26, 1.3, 2.6, and 3.9 W/kg). Immediately before microwave exposure, one or both eyes were treated topically with one drop of 0.5% timolol maleate or of 2% pilocarpine. Following administration of a drug, we observed a significant reduction in the power-density threshold (from 10 to 1 mW/cm2) for induction of corneal endothelial lesions and for increased vascular permeability of the iris. Diagnostic procedures (in vivo specular microscopy and fluorescein iris angiography) were performed following each exposure protocol. In addition, increased vascular permeability was confirmed with horseradish peroxidase tracer techniques. Although we did not measure intraocular temperatures in experimental animals, the results

suggest that a mechanism other than significant heating of the eye is involved. <u>Our data</u> indicate that pulsed microwaves at an average SAR of 0.26 W/kg, if administered after pretreatment with ophthalmic drugs, can produce significant ocular effects in the anesthetized primate.

#### Kojima M, Hata I, Wake K, Watanabe S, Yamanaka Y, Kamimura Y, Taki M, Sasaki K. Influence of anesthesia on ocular effects and temperature in rabbit eyes exposed to microwaves. Bioelectromagnetics 25(3):228-233, 2004.

To investigate the effect of systemic anesthesia on ocular effects and temperature in rabbit eyes exposed to microwaves, one eye each of 43 male pigmented rabbits (Dutch, 1.8-2.2 kg) was exposed at 2.45 GHz for 60-20 min (300 mW/cm2; 108 W/kg), either under anesthesia (ketamine hydrochloride (5 mg/kg) + xylazine (0.23 mg/kg)) or without anesthesia. Changes in the anterior segment were evaluated by image analysis utilizing a Scheimpflug camera, specular microscopy, and a laser flare cell meter. Temperatures within the eye were measured during microwave exposure by a Fluoroptic thermometer. The exposed eyes showed miosis, conjunctival congestion, corneal edema, and an increase in the light scattering of the anterior shallow cortex in the pupillary area of the lens. The group under systemic anesthesia showed much stronger symptoms than those treated without anesthesia. All of the anterior ocular changes disappeared within a week. The highest temperature during exposure was in the vitreous, followed by the anterior chamber, and the retrobulbar cavity of the orbit. The ocular temperatures of the rabbits under systemic anesthesia were 2-9 degrees C higher than those without anesthesia. Body temperature showed an increase of 1 degrees C during the exposure. Acute high intensity microwave exposure temporarily induced anterior segments inflammation and lens changes. The more pronounced ocular effects in the anesthetized rabbits were associated with the significantly higher ocular temperatures in the anesthetized animals. The influence of systemic anesthesia on ocular changes should be considered.

## Yu Y, <u>Yao K</u>. Non-thermal cellular effects of lowpower microwave radiation on the lens and lens epithelial cells. J Int Med Res. 38(3):729-736, 2010.

Because of the increased use of modern radiofrequency devices, public concern about the possible health effects of exposure to microwave radiation has arisen in many countries. It is well established that high-power microwave radiation can induce cataracts via its thermal effects. It remains unclear whether low-power microwave radiation, especially at levels below the current exposure limits, is cataractogenic. This review summarizes studies on the biological effects of low-power microwave radiation on lens and lens epithelial cells (LECs). It has been reported that exposure affects lens transparency, alters cell proliferation and apoptosis, inhibits gap junctional intercellular communication, and induces genetic instability and stress responses in LECs. These results raise the question of whether the ambient microwave environment can induce non-thermal effects in the lens and whether such effects have potential health consequences. Further in vivo studies on the effects on the lens of exposure to lowpower microwave radiation are needed.

# <u>Balci M</u>, <u>Namuslu M</u>, <u>Devrim E</u>, <u>Durak I</u>. Effects of computer monitor-emitted radiation on oxidant/antioxidant balance in cornea and lens from rats. <u>Mol Vis.</u> 15:2521-2525, 2009.

PURPOSE: This study aims to investigate the possible effects of computer monitoremitted radiation on the oxidant/antioxidant balance in corneal and lens tissues and to observe any protective effects of vitamin C (vit C). METHODS: Four groups (PC monitor, PC monitor plus vitamin C, vitamin C, and control) each consisting of ten Wistar rats were studied. The study lasted for three weeks. Vitamin C was administered in oral doses of 250 mg/kg/day. The computer and computer plus vitamin C groups were exposed to computer monitors while the other groups were not. Malondialdehyde (MDA) levels and superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT) activities were measured in corneal and lens tissues of the rats. RESULTS: In corneal tissue, MDA levels and CAT activity were found to increase in the computer group compared with the control group. In the computer plus vitamin C group, MDA level, SOD, and GSH-Px activities were higher and CAT activity lower than those in the computer and control groups. Regarding lens tissue, in the computer group, MDA levels and GSH-Px activity were found to increase, as compared to the control and computer plus vitamin C groups, and SOD activity was higher than that of the control group. In the computer plus vitamin C group, SOD activity was found to be higher and CAT activity to be lower than those in the control group. <u>CONCLUSION: The results of this study suggest</u> that computer-monitor radiation leads to oxidative stress in the corneal and lens tissues, and that vitamin C may prevent oxidative effects in the lens.

# Lu L, Xu H, Wang X, Guo G.Increased nitric oxide synthase activity is essential for electromagnetic-pulse-induced blood-retinal barrier breakdown in vivo.Brain Res. 1264:104-10, 2009.

PURPOSE: To examine whether electromagnetic pulses (EMPs) affected the permeability of the blood-retinal barrier (BRB), gene expression of occludin and activity of nitric oxide synthase (NOS). METHODS: Sprague-Dawley (SD) rats were used and randomized into EMP and control groups. Retinas were removed immediately, and 2 h or 24 h after EMP radiation. BRB permeability was analyzed by transmission electron microscopy and Evans Blue staining. Retinal NOS activity and concentrations of nitrite and nitrate were measured. Occludin mRNA and protein levels were detected by RT-PCR and Western blotting. RESULTS: Exposure of SD rats to EMP resulted in increased BRB permeability, with the greatest decrease in occludin at 24 h. Moreover, this permeability defect was also correlated with significant increases in the formation of NO and induction of NOS activity in SD rats. Furthermore, we found that treatment with NOS inhibitor N-nitro-L-arginine methyl ester (L-NAME) blocked BRB breakdown and prevented the increase in NO formation and induction of NOS activity, as well as the decrease in occluding expression. **CONCLUSION:** Taken together, these results support the view that NOS-dependent NO production is an important factor that contributes to EMP-induced BRB dysfunction, and suggests that NOS induction may play an important role in BRB breakdown.

## <u>Wang KJ</u>, Yao K, Lu DQ. [Effects of different dose microwave radiation on protein components of cultured rabbit lens] <u>Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi.</u> 25(4):208-210, 2007.[Article in Chinese]

OBJECTIVE: To study the effects of different dose microwave radiation on protein components of cultured rabbit lens, and analyze the mechanisms of lens injury caused by microwave radiation. METHODS: Cultured rabbit lens were exposed to microwave radiation with frequency of 2450 MHz and power density of 0.25, 0.50, 1.00, 2.00, 5.00 mW/cm(2) for 8 hours in vitro. The transparency of lens was observed. Changes of protein concentration were detected after different lens protein components were extracted, including water-soluble protein (WSP), urea soluble protein (USP), alkali soluble protein (ASP) and sonicated protein (SP). The influence of microwave radiation on WSP was analyzed using SDS-PAGE electrophoresis and coomassie-blue staining. RESULTS: Transparency of lens decreased after radiation. There was obvious opacification of lens cortex after 5.00 mW/cm(2) microwave radiation for 8 hours. After 1.00, 2.00 and 5.00 mW/cm(2) radiation, the percentage of WSP decreased while USP increased obviously. There was no change of ASP. The percentage of SP decreased when the power of microwave was 5.00 mW/cm(2). The low molecular weight protein of WSP decreased while high molecular weight protein increased after microwave radiation. CONCLUSION: Microwave radiation higher than 1.00 mW/cm(2) can affect the proportion of WSP and USP in cultured rabbit lens, and cause changes of lens transparency and refractive power, which leads to lens opacity.

### **Children Health and Cell Phone Use**

Wang PW, Liu TL, Ko CH, Lin HC, Huang MF, Yeh YC, Yen CF. Association between Problematic Cellular Phone Use and Suicide: The Moderating Effect of Family Function and Depression. <u>Compr Psychiatry</u>. 2013 Oct 19. pii: S0010-440X(13)00282-4. doi: 10.1016/j.comppsych.2013.09.006. [Epub ahead of print]

BACKGROUND: Suicidal ideation and attempt among adolescents are risk factors for eventual completed suicide. Cellular phone use (CPU) has markedly changed the everyday lives of adolescents. Issues about how cellular phone use relates to adolescent mental health, such as suicidal ideation and attempts, are important because of the high rate of cellular phone usage among children in that age group. This study explored the association between problematic CPU and suicidal ideation and attempts among adolescents and investigated how family function and depression influence the association between problematic CPU and suicidal ideation and attempts. METHODS: A total of 5051 (2872 girls and 2179 boys) adolescents who owned at least one cellular phone completed the research questionnaires. We collected data on participants' CPU and suicidal behavior (ideation and attempts) during the past month as well as information on family function and history of depression. <u>RESULTS: Five hundred thirty-two adolescents (10.54%) had problematic CPU.</u>

The rates of suicidal ideation were 23.50% and 11.76% in adolescents with problematic CPU and without problematic CPU, respectively. The rates of suicidal attempts in both groups were 13.70% and 5.45%, respectively. Family function, but not depression, had a moderating effect on the association between problematic CPU and suicidal ideation and attempt. CONCLUSION: This study highlights the association between problematic CPU and suicidal ideation as well as attempts and indicates that good family function may have a more significant role on reducing the risks of suicidal ideation and attempts in adolescents with problematic CPU than in those without problematic CPU.

## Leena K, Tomi L, Arja RR. Intensity of mobile phone use and health compromising behaviours-how is information and communication technology connected to health-related lifestyle in adolescence? J Adolesc. 28(1):35-47, 2005.

The association of mobile phone use with health compromising behaviours (smoking, snuffing, alcohol) was studied in a survey comprising a representative sample of 14-16-year-olds ([Formula: see text]) in 2001. Mobile phone was used by 89% of respondents and by 13% for at least 1h daily. The intensity of use was positively associated with health compromising behaviours. The associations remained, although somewhat reduced, after including weekly spending money in the models. This study concludes that, at least in the present developmental level of communication technologies, intensive mobile phone use seems to be part of the same health-related lifestyle as health compromising behaviours.

# Redmayne M, <u>Smith E</u>, <u>Abramson MJ</u>. Adolescent in-school cellphone habits: a census of rules, survey of their effectiveness, and fertility implications. <u>Reprod Toxicol.</u> 32(3):354-359, 2011.

We explored school cellphone rules and adolescent exposure to cellphone microwave emissions during school with a census and survey, respectively. The data were used to assess health and policy implications through a review of papers assessing reproductive bio-effects after exposure to cellphone emissions, this being most relevant to students' exposure. All schools banned private use of cellphones in class. However, 43% of student participants admitted breaking this rule. A high-exposure group of risk-takers was identified for whom prohibited in-school use was positively associated with high texting rates, carrying the phone switched-on >10h/day, and in-pocket use. The fertility literature is inconclusive, but increasingly points towards significant time- and dose-dependent deleterious effects from cellphone exposure on sperm. Genotoxic effects have been demonstrated from 'non-thermal' exposures, but not consistently. There is sufficient evidence and expert opinion to warrant an enforced school policy removing cellphones from students during the day.

#### Redmayne M. New Zealand adolescents' cellphone and cordless phone user-habits: are they at increased risk of brain tumours already? A cross-sectional study. Environ Health. 12(1):5, 2013.

**BACKGROUND:** Cellphone and cordless phone use is very prevalent among early adolescents, but the extent and types of use is not well documented. This paper

explores how, and to what extent, New Zealand adolescents are typically using and exposed to active cellphones and cordless phones, and considers implications of this in relation to brain tumour risk, with reference to current research findings. METHODS: This cross-sectional study recruited 373 Year 7 and 8 school students with a mean age of 12.3 years (range 10.3-13.7 years) from the Wellington region of New Zealand. Participants completed a questionnaire and measured their normal body-to-phone texting distances. Main exposure-metrics included self-reported time spent with an active cellphone close to the body, estimated time and number of calls on both phone types, estimated and actual extent of SMS text-messaging, cellphone functions used and people texted. Statistical analyses used Pearson Chi2 tests and Pearson's correlation coefficient (r). Analyses were undertaken using SPSS version 19.0. RESULTS: Both cellphones and cordless phones were used by approximately 90% of students. A third of participants had already used a cordless phone for  $\geq$  7 years. In 4 years from the survey to mid-2013, the cordless phone use of 6% of participants would equal that of the highest Interphone decile (≥ 1640 hours), at the surveyed rate of use. High cellphone use was related to cellphone location at night, being woken regularly, and being tired at school. More than a third of parents thought cellphones carried a moderate-to-high health risk for their child. CONCLUSIONS: While cellphones were very popular for entertainment and social interaction via texting, cordless phones were most popular for calls. If their use continued at the reported rate, many would be at increased risk of specific brain tumours by their mid-teens, based on findings of the Interphone and Hardell-group studies.

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

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.

#### Pedersen W. [Mobile phones, web chat, and sex among Norwegian adolescents] Tidsskr Nor Laegeforen. 124(13-14):1756-1759, 2004. [article in Norwegian]

BACKGROUND: We investigated the associations between new interactive technology for communication, such as web chat or mobile phones, and sexual behaviour among Norwegian adolescents. MATERIALS AND METHODS: A representative sample of adolescents (age 13-18, N = 10,926) filled in a questionnaire during school hours; the response rate was 92%. RESULTS: Most adolescents have access to communication technology, but how much they use it varies. In particular with regard to mobile phones, a strong association to sexual behaviour was found. Among those who did not use the new technology, less than 10% reported having had intercourse while two out of three of the most active users reported intercourse. The associations remained significant when controls were made for age and a range of contextual, family, peer and individual factors. INTERPRETATION: Norwegian adolescents have changed their sexual behaviour over the last decade. The introduction and widespread use of new communication technology is one of the most salient changes over the same period. The findings suggest that this technology may in fact be of importance to teenagers' sexual socialisation.

# <u>Thomas S</u>, <u>Heinrich S</u>, <u>von Kries R</u>, <u>Radon K</u>. Exposure to radio-frequency electromagnetic fields and behavioural problems in Bavarian children and adolescents. <u>Eur J Epidemiol.</u> 25(2):135-141, 2010.

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.

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

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 1year 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.

Sudan M, Kheifets L, Arah O, Olsen J, Zeltzer L. Prenatal and Postnatal Cell Phone Exposures and Headaches in Children. Open Pediatr Med Journal. 6(2012):46-52, 2012. OBJECTIVE: Children today are exposed to cell phones early in life, and may be at the greatest risk if exposure is harmful to health. We investigated associations between cell phone exposures and headaches in children. STUDY DESIGN: The Danish National Birth Cohort enrolled pregnant women between 1996 and 2002. When their children reached age seven years, mothers completed a questionnaire regarding the child's health, behaviors, and exposures. We used multivariable adjusted models to relate prenatal only, postnatal only, or both prenatal and postnatal cell phone exposure to whether the child had migraines and headache-related symptoms. <u>RESULTS: Our analyses included data from 52,680 children</u>.

<u>Children with cell phone exposure had higher odds of migraines and headache-related</u> symptoms than children with no exposure. The odds ratio for migraines was 1.30 (95% confidence interval: 1.01-1.68) and for headache-related symptoms was 1.32 (95% confidence interval: 1.23-1.40) for children with both prenatal and postnatal exposure. CONCLUSIONS: In this study, cell phone exposures were associated with headaches in children, but the associations may not be causal given the potential for uncontrolled confounding and misclassification in observational studies such as this. However, given the widespread use of cell phones, if a causal effect exists it would have great public health impact.

# 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.

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.

#### Krause CM, Bjornberg CH, Pesonen M, Hulten A, Liesivuori T, Koivisto M, Revonsuo A, Laine M, Hamalainen H. Mobile phone effects on children's event-related oscillatory EEG during an auditory memory task. Int J Radiat Biol. 82(6):443-450, 2006. Purpose: To assess the effects of electromagnetic fields (EMF) emitted by mobile phones (MP) on the 1 - 20 Hz event-related brain oscillatory EEG (electroencephalogram) responses in children performing an auditory memory task (encoding and recognition).Materials and methods: EEG data were gathered while 15 subjects (age 10 - 14 years) performed an auditory memory task both with and without exposure to a digital 902 MHz MP in counterbalanced order.Results: During memory encoding, the active MP modulated the event-related desynchronization/synchronization (ERD/ERS) responses in the approximately 4 - 8 Hz EEG frequencies. During recognition, the active MP transformed these brain oscillatory responses in the approximately 4 - 8 Hz and approximately 15 Hz frequencies.Conclusions: The current findings suggest that EMF emitted by mobile

phones has effects on brain oscillatory responses during cognitive processing in children.

Kamibeppu K, Sugiura H. Impact of the mobile phone on junior high-school students' friendships in the Tokyo metropolitan area. Cyberpsychol Behav. 8(2):121-130, 2005. The proportion of having keitai (Japanese mobile phone) has increased rapidly in young children. To research how junior high school students use their own keitai and to examine the impact of using it on their psychology, especially on their friendship, we recruited 651 students, grade 8, from five public junior high schools in the Tokyo metropolitan area. Each student participant completed a questionnaire that we had created. The response rates were 88.8% (n = 578) for participants. The proportion of having their own keitai was 49.3% (n = 285) and that of not having it was 50.7% (n = 293). We found that they used it much more frequently for e-mail than as a phone. Most of them exchanged e-mails between schoolmates, and more than a half of them exchanged e-mails more than 10 times a day. Sociable students estimated that their own keitai was useful for their friendship. But they experienced some insecurity or started staying up late at night engaged in e-mail exchanges, and they thought that they could not live without their own keitai. Our findings suggest that keitai having an e-mail function play a big part in the junior high-school students' daily life, and its impact on students' friendships, psychology, or health should be discussed among students to prevent keitai addiction.

# <u>Soderqvist F</u>, <u>Carlberg M</u>, <u>Hardell L</u>. Use of wireless telephones and self-reported health symptoms: a population-based study among Swedish adolescents aged 15-19 years. <u>Environ Health.</u> 7(1):18, 2008.

ABSTRACT: BACKGROUND: Despite the last years of rapid increase in use of wireless phones little data on the use of these devices has been systematically assessed among young persons. The aim of this descriptive cross-sectional study was to assess use of wireless phones and to study such use in relation to explanatory factors and selfreported health symptoms. METHODS: A postal questionnaire comprising 8 pages of 27 questions with 75 items in total was sent to 2000 Swedish adolescents aged 15-19 years and selected from the population registry using a stratified sampling scheme. RESULTS: The questionnaire was answered by 63.5 % of the study subjects. Most participants reported access to a mobile phone (99.6%) and use increased with age; 55.6% of the 15year-olds and 82.2% of the 19-year-olds were regular users. Girls generally reported more frequent use than boys. Use of wired hands-free equipment 'anytime' was reported by 17.4%. Cordless phones were used by 81.9%, and 67.3% were regular users. Watching TV increased the odds ratio for use of wireless phones, adjusted for age and gender. Some of the most frequently reported health complaints were tiredness, stress, headache, anxiety, concentration difficulties and sleep disturbances. Regular users of wireless phones had health symptoms more often and reported poorer perceived health than less frequent users. CONCLUSIONS: Almost all adolescence in this study used a wireless phone, girls more than boys. The most frequent use was seen among the older adolescents and those who watched TV extensively. The study further showed that

perceived health and certain health symptoms seemed to be related to the use of wireless phones. However, this part of the investigation was explorative and should therefore be interpreted with caution since bias and chance findings due to multiple testing might have influenced the results. Potentially this study will stimulate more sophisticated studies that may also investigate directions of associations and whether, or to what degree, any mediation factors are involved.

## <u>Schuz J</u>. Mobile phone use and exposures in children. Bioelectromagnetics. Suppl 7:S45-50,2005.

The main difference concerning the use of mobile phones (MPs) between today's children and adults is the longer lifetime exposure of children when they grow older, due to starting to use MPs at an early age. Additionally, recent trends lead to a higher frequency of use among children, including higher popularity of MPs and features specifically designed to attract children. The prevalence of MP users is already very high and reaches >90% among adolescents in some countries. In a German study, 6% of 9-10 years old children used a MP for making calls daily; 35% owned their own MP. For children, MPs are dominant sources of radio wave exposures and relevant sources of extremely low frequency magnetic fields. For very young children, however, environmental exposure to radio waves may be of concern. In conclusion, children will have a much higher cumulative exposure to radio waves than today's adults when they are at the same age. Radio wave exposure of children may be estimated more easily, because the variety of exposure sources is smaller than for adults. As long as adverse health effects cannot be ruled out with some degree of certainty, it appears to be appropriate to instruct children and their parents about a prudent use of MPs.

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

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. <u>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 significant higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during significant higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during develops of the higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (other the prosure in the highest quartile during higher intensity of headache (o</u>

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.

#### 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 populationbased cross-sectional study. BMC Public Health. 2014 Oct 1;14(1):1022. [Epub ahead of print]

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 crosssectional 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 crosssectional 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.

# Chiu CT, Chang YH, Chen CC, Ko MC, Li CY. Mobile phone use and health symptoms in children. J Formos Med Assoc. 2014 Aug 9. pii: S0929-6646(14)00207-1. doi: 10.1016/j.jfma.2014.07.002. [Epub ahead of print]

BACKGROUND/PURPOSE: To investigate the mobile phone (MP) use for talking in relation to health symptoms among 2042 children aged 11-15 years in Taiwan. METHODS: A nationwide, cross-sectional study, using the computer assisted telephone interview (CATI) technique, was conducted in 2009 to collect information on children's utilization of MPs and the perceived health symptoms reported by their parents. <u>RESULTS: The overall prevalence of MP use in the past month was estimated at 63.2%</u> [95% confidence interval (CI) = 61.1-65.3%]. MP use was associated with a significantly increased adjusted odds ratio (AOR) for headaches and migraine (1.42, 95% CI = 1.12-1.81) and skin itches (1.84, 95% CI = 1.47-2.29). Children who regularly used MPs were also considered to have a health status worse than it was 1 year ago ( $\beta$  = 0.27, 95% CI =

<u>0.17-0.37</u>). CONCLUSION: Although the cross-sectional design precludes the causal inference for the observed association, <u>our study tended to suggest a need for more cautious use of MPs in children, because children are expected to experience a longer lifetime exposure to radiofrequency electromagnetic fields (RF-EMF) from MPs.</u>

Peyman A, Rezazadeh AA, Gabriel C. Changes in the dielectric properties of rat tissue as a function of age at microwave frequencies. Phys Med Biol 46(6):1617-1629, 2001. The dielectric properties of ten rat tissues at six different ages were measured at 37 degrees C in the frequency range of 130 MHz to 10 GHz using an open-ended coaxial probe and a computer controlled network analyser. The results show a general decrease of the dielectric properties with age. The trend is more apparent for brain, skull and skin tissues and less noticeable for abdominal tissues. The variation in the dielectric properties with age is due to the changes in the water content and the organic composition of tissues. The percentage decrease in the dielectric properties of certain tissues in the 30 to 70 day old rats at cellular phone frequencies have been tabulated. These data provide an important input in the provision of rigorous dosimetry in lifetimeexposure animal experiments. The results provide some insight into possible differences in the assessment of exposure for children and adults.

#### de Salles <u>AA</u>, <u>Bulla G</u>, <u>Rodriguez CE</u>. Electromagnetic absorption in the head of adults and children due to mobile phone operation close to the head. <u>Electromagn Biol Med.</u> 2006;25(4):349-360, 2006.

The Specific Absorption Rate (SAR) produced by mobile phones in the head of adults and children is simulated using an algorithm based on the Finite Difference Time Domain (FDTD) method. Realistic models of the child and adult head are used. The electromagnetic parameters are fitted to these models. Comparison also are made with the SAR calculated in the children model when using adult human electromagnetic parameters values. Microstrip (or patch) antennas and quarter wavelength monopole antennas are used in the simulations. The frequencies used to feed the antennas are 1850 MHz and 850 MHz. The SAR results are compared with the available international recommendations. It is shown that under similar conditions, the 1g-SAR calculated for children is higher than that for the adults. When using the 10-year old child model, SAR values higher than 60% than those for adults are obtained.

## <u>Peyman A</u>, <u>Holden SJ</u>, <u>Watts S</u>, <u>Perrott R</u>, <u>Gabriel C</u>. Dielectric properties of porcine cerebrospinal tissues at microwave frequencies: in vivo, in vitro and systematic variation with age. <u>Phys Med Biol</u>. 52(8):2229-2245, 2007.

The dielectric properties of pig cerebrospinal tissues were measured in vivo and in vitro, in the frequency range of 50 MHz-20 GHz. The total combined measurement uncertainty was calculated at each frequency point and is reported over representative frequency regions. Comparisons were made for each tissue between the two sets of data and with the literature of the past decade. The in vitro study was extended to include tissue from pigs weighing approximately 10, 50 and 250 kg to re-visit the question of the variation of dielectric properties with age. <u>White matter and spinal</u>

<u>chord showed significant variation as function of animal age, no age-related variations</u> were recorded for grey matter.

### **Effects on Behavior**

Shtemberg AS, Uzbekov MG, Shikhov SN, Bazian AS, Cherniakov GM, [Species specificity, age factors, and various neurochemical correlates of the animal spontaneous behavior after exposure to electromagnetic field of the ultralow intensity]. *Zh Vyssh Nerv Deiat Im I P Pavlova* 50(4):703-715, 2000. [Article in Russian] Behavioral and neurochemical reactions of small laboratory animals (mice and rats of different age) under exposure to ultralow-intensity electromagnetic fields (EMF, frequency of 4200 and 970 MHz, modulated by a quasistochastic signal in the range of 20-20,000 Hz, power density 15 microW/cm2, specific body absorption rate up to 4.5 mJ/kg) were studied. The EMF basically inhibited the locomotor and exploratory activity in the "open-field" test. The species- and age-specific features rather than radiation conditions dominated. However, decrease in the EMF frequency considerably intensified the observed effect. Change in animal behavior was accompanied by shifts in neurochemical processes, i.e., sharp activation of serotoninergic and inhibition of morepinephrinergic system.

# 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.

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  $\mu$ W/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.

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. 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."

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

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).

#### 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. <u>Neurol Res.</u> 2014 Jan 27:1743132813Y000000276. [Epub ahead of print]

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 <u>stress behavior actions were observe</u>. <u>Conclusion:</u> <u>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.</u>

#### 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. 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.

## <u>Divan HA</u>, <u>Kheifets L</u>, <u>Obel C</u>, <u>Olsen J</u>. Cell phone use and behavioural problems in young children. <u>J Epidemiol Community Health.</u>66(6):524-529, 2012.

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 7years. 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). <u>Conclusions: The</u> <u>findings of the previous publication were replicated in this separate group of</u> <u>participants demonstrating that cell phone use was associated with behavioural</u> <u>problems at age 7years in children, and this association was not limited to early users of</u> <u>the technology.</u> Although weaker in the new dataset, even with further control for an extended set of potential confounders, the associations remained.

# **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

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 nonsignificant 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.

#### Razavinasab M, Moazzami K, Shabani M. Maternal mobile phone exposure alters intrinsic electrophysiological properties of CA1 pyramidal neurons in rat offspring. Toxicol Ind Health. 2014 Mar 6. [Epub ahead of print]

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. <u>The</u> results of the passive avoidance and Morris water maze assessment of learning and <u>memory performance showed that phone exposure significantly altered learning</u> <u>acquisition and memory retention in male and female rats compared with the control</u> <u>rats.</u> Light microscopy study of brain sections of the control and mobile phone-exposed rats showed normal morphology.<u>Our results suggest that exposure to mobile phones</u> <u>adversely affects the cognitive performance of both female and male offspring rats</u> <u>using behavioral and electrophysiological techniques.</u>

#### <u>Valentini E</u>, <u>Ferrara M</u>, <u>Presaghi F</u>, <u>De Gennaro L</u>, <u>Curcio G</u>. Republished review: systematic review and meta-analysis of psychomotor effects of mobile phone electromagnetic fields.<u>Postgrad Med J.</u> 87(1031):643-651, 2011.

OBJECTIVES Over the past 10 years there has been increasing concern about the possible behavioural effects of mobile phone use. This systematic review and metaanalysis focuses on studies published since 1999 on the human cognitive and performance effects of mobile phone-related electromagnetic fields (EMF). METHODS PubMed, Biomed, Medline, Biological Sciences, PsychInfo, PsycARTICLES, Environmental Sciences and Pollution Management, Neurosciences Abstracts and Web of Science professional databases were searched and 24 studies selected for meta-analysis. Each study had to have at least one psychomotor measurement result as a main outcome. Data were analysed using standardised mean difference (SMD) as the effect size measure. RESULTS Only three tasks (2-back, 3-back and simple reaction time (SRT)) displayed significant heterogeneity, but after studies with extreme SMD were excluded using sensitivity analysis, the statistical significance disappeared ( $\chi(2)(7)=1.63$ , p=0.20;  $\chi(2)(6)=1.00$ , p=0.32;  $\chi(2)(10)=14.04$ , p=0.17, respectively). Following sensitivity analysis, the effect of sponsorship and publication bias were assessed. Meta-regression indicated a significant effect (b1/40.12, p<0.05) only for the 2-back task with mixed funding (industry and public/charity). Funnel plot inspection revealed a significant publication bias only for two cognitive tasks: SRT (Begg's rank correlation r=0.443; Egger's test b=-0.652) and the subtraction task (Egger's test b=-0.687). CONCLUSIONS Mobile phonelike EMF do not seem to induce cognitive and psychomotor effects. Nonetheless, the existence of sponsorship and publication biases should encourage WHO intervention to develop official research standards and guidelines. In addition, future research should address critical and neglected issues such as investigation of repeated, intensive and chronic exposures, especially in highly sensitive populations such as children.

#### <u>Thomas S</u>, <u>Heinrich S</u>, <u>von Kries R</u>, <u>Radon K</u>. **Exposure to radio-frequency** electromagnetic fields and behavioural problems in Bavarian children and adolescents. <u>Eur J Epidemiol.</u> 25(2):135-141, 2010.

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.

#### 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.

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.

<u>Hirata A</u>, <u>Kojima M</u>, <u>Kawai H</u>, <u>Yamashiro Y</u>, <u>Watanabe S</u>, <u>Sasaki H</u>, <u>Fujiwara O</u>. Acute dosimetry and estimation of threshold inducing behavioral signs of thermal stress in

rabbits at 2.45-GHz microwave exposure. IEEE Trans Biomed Eng. 57(5):1234-42, 2010.

In the current international guidelines and standards for human exposure to microwaves, the basic restriction is determined by the whole-body average specific absorption rate (SAR). The basis for the guidelines is the adverse effect such as work stoppage in animals for whole-body average SARs above a certain level. Although it is known that absorbed microwave energy causes the behavioral sign of thermal stress, the relationship of whole-body average SAR with temperature/temperature elevation has not been sufficiently investigated. In the present study, we performed experiments on rabbits exposed to 2.45-GHz microwaves. A total of 24 measurements were conducted for power densities from approximately 100 to 1,000 W/m2. Our computational code for electromagnetic-thermal dosimetry was used to set the exposure time duration and incident power density. Our experimental results suggest that a core temperature elevation of 1oC is an estimate of the threshold inducing complex behavioral signs of microwave-induced thermal stress in rabbits for different whole-body average SARs and exposure time durations. The whole-body average SAR required for microwave-induced behavioral sign in rabbits was estimated as approximately 1.3 W/kg for 2.45-GHz microwaves.

## Duan L, Shan Y, Yu X, [Observations of changes in neurobehavioral functions in workers exposed to high-frequency radiation]. Chung Hua Yu Fang I Hsueh Tsa Chih 32(2):109-111, 1998. [Article in Chinese]

OBJECTIVE: To study the effects of exposure to high-frequency radiation on neurobehavioral function of the exposed workers and its measurement in evaluating occupational hazards caused by it. METHODS: Four neurobehavioral functions were tested for the workers exposed to high-frequency radiation with Neurobehavioral Core Tests Battery recommended by WHO. <u>RESULTS: Scores for various indicators in exposed workers were significantly lower than those in controls, and correlated to the detection of neurobehavioral function in workers exposed to high-frequency radiation can reflect its important adverse effects.</u>

### **Electromagnetic Hypersensitivity**

# Nordin S, Neely G, Olsson D, Sandström M. Odor and Noise Intolerance in Persons with Self-Reported Electromagnetic Hypersensitivity. Int J Environ Res Public Health. 11(9):8794-8805, 2014.

Lack of confirmation of symptoms attributed to electromagnetic fields (EMF) and triggered by EMF exposure has highlighted the role of individual factors. Prior observations indicate intolerance to other types of environmental exposures among persons with electromagnetic hypersensitivity (EHS). This study assessed differences in odor and noise intolerance between persons with EHS and healthy controls by use of subscales and global measures of the Chemical Sensitivity Scale (CSS) and the Noise

Sensitivity Scale (NSS). The EHS group scored significantly higher than the controls on all CSS and NSS scales. Correlation coefficients between CSS and NSS scores ranged from 0.60 to 0.65 across measures. The findings suggest an association between EHS and odor and noise intolerance, encouraging further investigation of individual factors for understanding EMF-related symptoms.

### <u>Wilen J</u>, <u>Johansson A</u>, <u>Kalezic N</u>, <u>Lyskov E</u>, <u>Sandstrom M</u>. Psychophysiological tests and provocation of subjects with mobile phone related symptoms. <u>Bioelectromagnetics</u>.27(3):204-214, 2006.

The aim of the present study was to investigate the effect of exposure to a mobile phone-like radiofrequency (RF) electromagnetic field on persons experiencing subjective symptoms when using mobile phones (MP). Twenty subjects with MP-related symptoms were recruited and matched with 20 controls without MP-related symptoms. Each subject participated in two experimental sessions, one with true exposure and one with sham exposure, in random order. In the true exposure condition, the test subjects were exposed for 30 min to an RF field generating a maximum SAR(1g) in the head of 1 W/kg through an indoor base station antenna attached to a 900 MHz GSM MP. The following physiological and cognitive parameters were measured during the experiment: heart rate and heart rate variability (HRV), respiration, local blood flow, electrodermal activity, critical flicker fusion threshold (CFFT), short-term memory, and reaction time. No significant differences related to RF exposure conditions were detected. Also no differences in baseline data were found between subject groups, except for the reaction time, which was significantly longer among the cases than among the controls the first time the test was performed. This difference disappeared when the test was repeated. However, the cases differed significantly from the controls with respect to HRV as measured in the frequency domain. The cases displayed a shift in low/high frequency ratio towards a sympathetic dominance in the autonomous nervous system during the CFFT and memory tests, regardless of exposure condition. This might be interpreted as a sign of differences in the autonomous nervous system regulation between persons with MP related subjective symptoms and persons with no such symptoms.

## <u>Kato Y</u>, <u>Johansson O</u>. Reported functional impairments of electrohypersensitive Japanese: A questionnaire survey. <u>Pathophysiology.</u>19(2) 95-100, 2012.

An increasing number of people worldwide complain that they have become electromagnetic hypersensitive (EHS). We conducted a questionnaire survey of EHS persons in Japan. The aim was to identify electromagnetic fields (EMF) and plausible EMF sources that caused their symptoms. Postal questionnaires were distributed via a self-help group, and 75 participants (95% women) responded. Reported major complaints were "fatigue/tiredness" (85%), "headache", "concentration, memory, and thinking" difficulty (81%, respectively). Seventy-two per cent used some form of complementary/alternative therapy. The most plausible trigger of EHS onset was a mobile phone base station or personal handy-phone system (37%). Sixty-five percent experienced health problems to be due to the radiation from other passengers' mobile phones in trains or buses, and 12% reported that they could not use public

transportation at all. Fifty-three percent had a job before the onset, but most had lost their work and/or experienced a decrease in income. Moreover, 85.3% had to take measures to protect themselves from EMF, such as moving to low EMF areas, or buying low EMF electric appliances. <u>EHS persons were suffering not only from their symptoms, but also from economical and social problems.</u>

# <u>Johansson A</u>, <u>Nordin S</u>, <u>Heiden M</u>, <u>Sandström M</u>. Symptoms, personality traits, and stress in people with mobile phone-related symptoms and electromagnetic hypersensitivity. <u>J Psychosom Res.</u> 68(1):37-45, 2010.

OBJECTIVE: Some people report symptoms that they associate with electromagnetic field (EMF) exposure. These symptoms may be related to specific EMF sources or to electrical equipment in general (perceived electromagnetic hypersensitivity, EHS). Research and clinical observations suggest a difference between mobile phone (MP)related symptoms and EHS with respect to symptom prevalence, psychological factors, and health prognosis. This study assessed prevalence of EMF-related and EMFnonrelated symptoms, anxiety, depression, somatization, exhaustion, and stress in people with MP-related symptoms or EHS versus a population-based sample and a control sample without EMF-related symptoms. METHODS: Forty-five participants with MP-related symptoms and 71 with EHS were compared with a population-based sample (n=106) and a control group (n=63) using self-report questionnaires. RESULTS: The EHS group reported more symptoms than the MP group, both EMF-related and EMFnonrelated. The MP group reported a high prevalence of somatosensory symptoms, whereas the EHS group reported more neurasthenic symptoms. As to self-reported personality traits and stress, the case groups differed only on somatization and listlessness in a direct comparison. In comparison with the reference groups, the MP group showed increased levels of exhaustion and depression but not of anxiety, somatization, and stress; the EHS group showed increased levels for all of the conditions except for stress. CONCLUSION: The findings support the idea of a difference between people with symptoms related to specific EMF sources and people with general EHS with respect to symptoms and anxiety, depression, somatization, exhaustion, and stress. The differences are likely to be important in the management of patients.

# Hagström M, Auranen J, Ekman R. Electromagnetic hypersensitive Finns: Symptoms, perceived sources and treatments, a questionnaire study. Pathophysiology. 2013 Apr 1. pii: S0928-4680(13)00002-3.

The aim was to analyze the subjective experiences of Finns who describe themselves as suffering from electromagnetic hypersensitivity (EHS), their symptoms, self-perceived sources of the health complaints and the effectiveness of medical and complementary alternative therapies. A total of 395 questionnaires were mailed to self-diagnosed EHS persons. Of the participants 345 belonged to a Finnish self-help group and 50 came from outside of the group. The return rate of the study was 52.1% (206) and 80.9% of the respondents were women. Before the onset of EHS the most common health complaints were different types of allergies (35.1%, 68). During the acute phase of EHS the most common symptoms were nervous system related: "stress" (60.3%, 117),

"sleeping disorders" (59.3%, 115) and "fatigue" (57.2%, 111). The sources that were most often reported to have triggered EHS were: "personal computers" (50.8%, 94) and "mobile phones" (47.0%, 87). The same devices were also claimed to cause the most symptoms during the acute phase. After the acute phase of EHS had passed, the respondents still claimed to react to these same digital and wireless devices while their reactions to basic electrical appliances were reduced. According to 76% of 157 respondents the reduction or avoidance of electromagnetic fields (EMF) helped in their full or partial recovery. The best treatments for EHS were given as: "dietary change" (69.4%), "nutritional supplements" (67.8%) and "increased physical exercise" (61.6%). The official treatment recommendations of psychotherapy (2.6%) and medication (-4.2%) were not significantly helpful. According to the present results the official treatment protocols should take better account the EHS person's own experiences. The avoidance of electromagnetic radiation and fields effectively removed or lessened the symptoms in EHS persons.

#### De Luca C, Chung Sheun Thai J, Raskovic D, Cesareo E, Caccamo D, Trukhanov A, Korkina L. Metabolic and genetic screening of electromagnetic hypersensitive subjects as a feasible tool for diagnostics and intervention. Mediators Inflamm. 2014;2014:924184. doi: 10.1155/2014/924184. Epub 2014 Apr 9.

Growing numbers of "electromagnetic hypersensitive" (EHS) people worldwide selfreport severely disabling, multiorgan, non-specific symptoms when exposed to low-dose electromagnetic radiations, often associated with symptoms of multiple chemical sensitivity (MCS) and/or other environmental "sensitivity-related illnesses" (SRI). This cluster of chronic inflammatory disorders still lacks validated pathogenetic mechanism, diagnostic biomarkers, and management guidelines. We hypothesized that SRI, not being merely psychogenic, may share organic determinants of impaired detoxification of common physic-chemical stressors. Based on our previous MCS studies, we tested a panel of 12 metabolic blood redox-related parameters and of selected drugmetabolizing-enzyme gene polymorphisms, on 153 EHS, 147 MCS, and 132 control Italians, confirming MCS altered (P < 0.05-0.0001) glutathione-(GSH), GSH-peroxidase/Stransferase, and catalase erythrocyte activities. We first described comparable-though milder-metabolic pro-oxidant/proinflammatory alterations in EHS with distinctively increased plasma coenzyme-Q10 oxidation ratio. Severe depletion of erythrocyte membrane polyunsaturated fatty acids with increased  $\omega$  6/ $\omega$  3 ratio was confirmed in MCS, but not in EHS. We also identified significantly (P = 0.003) altered distributionversus-control of the CYP2C19\*1/\*2 SNP variants in EHS, and a 9.7-fold increased risk (OR: 95% C.I. = 1.3-74.5) of developing EHS for the haplotype (null)GSTT1 + (null)GSTM1 variants. Altogether, results on MCS and EHS strengthen our proposal to adopt this blood metabolic/genetic biomarkers' panel as suitable diagnostic tool for SRI.

# Nordin S, Neely G, Olsson D, Sandström M. Odor and Noise Intolerance in Persons with Self-Reported Electromagnetic Hypersensitivity. Int J Environ Res Public Health. 11(9):8794-8805, 2014.

Lack of confirmation of symptoms attributed to electromagnetic fields (EMF) and

triggered by EMF exposure has highlighted the role of individual factors. Prior observations indicate intolerance to other types of environmental exposures among persons with electromagnetic hypersensitivity (EHS). This study assessed differences in odor and noise intolerance between persons with EHS and healthy controls by use of subscales and global measures of the Chemical Sensitivity Scale (CSS) and the Noise Sensitivity Scale (NSS). The EHS group scored significantly higher than the controls on all CSS and NSS scales. Correlation coefficients between CSS and NSS scores ranged from 0.60 to 0.65 across measures. <u>The findings suggest an association between EHS and</u> odor and noise intolerance, encouraging further investigation of individual factors for <u>understanding EMF-related symptoms.</u>

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### Landgrebe M, Hauser S, Langguth B, Frick U, Hajak G, Eichhammer P. Altered cortical excitability in subjectively electrosensitive patients: results of a pilot study. J Psychosom Res. 62(3):283-288, 2007.

OBJECTIVE: Hypersensitivity to electromagnetic fields is frequently claimed to be linked to a variety of unspecific somatic and/or neuropsychological complaints. Whereas provocation studies often failed to demonstrate a causal relationship between electromagnetic field exposure and symptom formation, neurophysiological examinations highlight baseline deviations in people claiming to be electrosensitive. METHODS: To elucidate a potential role of dysfunctional cortical regulations in mediating hypersensitivity to electromagnetic fields, cortical excitability parameters were measured by transcranial magnetic stimulation in subjectively electrosensitive patients (n=23) and two control groups (n=49) differing in their level of unspecific health complaints. <u>RESULTS: Electrosensitive patients showed reduced intracortical facilitation as compared to both control groups, while motor thresholds and intracortical inhibition were unaffected. CONCLUSIONS: This pilot study gives additional evidence that altered central nervous system function may account for symptom manifestation in subjectively electrosensitive patients as has been postulated for several chronic multisymptom illnesses sharing a similar clustering of symptoms.</u>

# Hagström M, Auranen J, Ekman R. Electromagnetic hypersensitive Finns: Symptoms, perceived sources and treatments, a questionnaire study. Pathophysiology. 2013 Apr 1. pii: S0928-4680(13)00002-3.

The aim was to analyze the subjective experiences of Finns who describe themselves as suffering from electromagnetic hypersensitivity (EHS), their symptoms, self-perceived sources of the health complaints and the effectiveness of medical and complementary alternative therapies. A total of 395 guestionnaires were mailed to self-diagnosed EHS persons. Of the participants 345 belonged to a Finnish self-help group and 50 came from outside of the group. The return rate of the study was 52.1% (206) and 80.9% of the respondents were women. Before the onset of EHS the most common health complaints were different types of allergies (35.1%, 68). During the acute phase of EHS the most common symptoms were nervous system related: "stress" (60.3%, 117), "sleeping disorders" (59.3%, 115) and "fatigue" (57.2%, 111). The sources that were most often reported to have triggered EHS were: "personal computers" (50.8%, 94) and "mobile phones" (47.0%, 87). The same devices were also claimed to cause the most symptoms during the acute phase. After the acute phase of EHS had passed, the respondents still claimed to react to these same digital and wireless devices while their reactions to basic electrical appliances were reduced. According to 76% of 157 respondents the reduction or avoidance of electromagnetic fields (EMF) helped in their full or partial recovery. The best treatments for EHS were given as: "dietary change" (69.4%), "nutritional supplements" (67.8%) and "increased physical exercise" (61.6%). The official treatment recommendations of psychotherapy (2.6%) and medication (-4.2%) were not significantly helpful. According to the present results the official treatment protocols should take better account the EHS person's own experiences. The avoidance of electromagnetic radiation and fields effectively removed or lessened the symptoms in EHS persons.

#### <u>Landgrebe M</u>, <u>Frick U</u>, <u>Hauser S</u>, <u>Langguth B</u>, <u>Rosner R</u>, <u>Hajak G</u>, <u>Eichhammer P</u>. **Cognitive and neurobiological alterations in electromagnetic hypersensitive patients: results of a case-control study.** <u>Psychol Med.</u> **38(12):1781-1791, 2008**.

BACKGROUND: Hypersensitivity to electromagnetic fields (EMF) is frequently claimed to be linked to a variety of non-specific somatic and neuropsychological complaints. Whereas provocation studies often failed to demonstrate a causal relationship between EMF exposure and symptom formation, recent studies point to a complex interplay of neurophysiological and cognitive alterations contributing to symptom manifestation in electromagnetic hypersensitive patients (EHS). However, these studies have examined only small sample sizes or have focused on selected aspects. Therefore this study examined in the largest sample of EHS EMF-specific cognitive correlates, discrimination ability and neurobiological parameters in order to get further insight into the pathophysiology of electromagnetic hypersensitivity. METHOD: In a case-control design 89 EHS and 107 age- and gender-matched controls were included in the study. Health status and EMF-specific cognitions were evaluated using standardized questionnaires. Perception thresholds following single transcranial magnetic stimulation (TMS) pulses to

the dorsolateral prefrontal cortex were determined using a standardized blinded measurement protocol. Cortical excitability parameters were measured by TMS. RESULTS: Discrimination ability was significantly reduced in EHS (only 40% of the EHS but 60% of the controls felt no sensation under sham stimulation during the complete series), whereas the perception thresholds for real magnetic pulses were comparable in both groups (median 21% versus 24% of maximum pulse intensity). Intra-cortical facilitation was decreased in younger and increased in older EHS. In addition, typical EMF-related cognitions (aspects of rumination, symptom intolerance, vulnerability and stabilizing self-esteem) specifically differentiated EHS from their controls. <u>CONCLUSIONS: These results demonstrate significant cognitive and neurobiological</u> <u>alterations pointing to a higher genuine individual vulnerability of electromagnetic</u> <u>hypersensitive patients.</u>

### Landgrebe M, Frick U, Hauser S, Hajak G, Langguth B. Association of tinnitus and electromagnetic hypersensitivity: hints for a shared pathophysiology? <u>PLoS</u> <u>One.</u>4(3):e5026, 2009.

BACKGROUND: Tinnitus is a frequent condition with high morbidity and impairment in quality of life. The pathophysiology is still incompletely understood. Electromagnetic fields are discussed to be involved in the multi-factorial pathogenesis of tinnitus, but data proofing this relationship are very limited. Potential health hazards of electromagnetic fields (EMF) have been under discussion for long. Especially, individuals claiming themselves to be electromagnetic hypersensitive suffer from a variety of unspecific symptoms, which they attribute to EMF-exposure. The aim of the study was to elucidate the relationship between EMF-exposure, electromagnetic hypersensitivity and tinnitus using a case-control design. METHODOLOGY: Tinnitus occurrence and tinnitus severity were assessed by questionnaires in 89 electromagnetic hypersensitive patients and 107 controls matched for age-, gender, living surroundings and workplace. Using a logistic regression approach, potential risk factors for the development of tinnitus were evaluated. FINDINGS: Tinnitus was significantly more frequent in the electromagnetic hypersensitive group (50.72% vs. 17.5%) whereas tinnitus duration and severity did not differ between groups. Electromagnetic hypersensitivity and tinnitus were independent risk factors for sleep disturbances. However, measures of individual EMF-exposure like e.g. cell phone use did not show any association with tinnitus. CONCLUSIONS: Our data indicate that tinnitus is associated with subjective electromagnetic hypersensitivity. An individual vulnerability probably due to an over activated cortical distress network seems to be responsible for, both, electromagnetic hypersensitivity and tinnitus. Hence, therapeutic efforts should focus on treatment strategies (e.g. cognitive behavioral therapy) aiming at normalizing this dysfunctional distress network.

### **Effects on Wellbeing**

### Szyjkowska A, Gadzicka E, Szymczak W, Bortkiewicz A. The risk of subjective symptoms in mobile phone users in Poland - An epidemiological study. Int J Occup Med Environ Health. 2014 Apr 1. [Epub ahead of print]

**OBJECTIVES:** To assess the type and incidence of subjective symptoms related to the use of mobile phones in Polish users. MATERIAL AND METHODS: The study was conducted in 2005 using a questionnaire survey. Although it has been quite a long time, up to now, no such data have been published for Poland. The questionnaire consisted of 53 questions concerning sex, age, education, general health, characteristics of a mobile phone (hand-held, loud-speaking unit) as well as the habits associated with its use (frequency and duration of calls, text messages, etc.) and complaints associated with using a mobile phone. RESULTS: As many as 1800 questionnaires were sent. The response was obtained from 587 subjects aged 32.6±11.3 (48.9% women, 51.1% men); the age did not differ significantly between men and women. The subjects owned a cell phone for an average of 3 years. Majority of the respondents used the phone intensively, i.e. daily (74%) or almost daily (20%). Headaches were reported significantly more often by the people who talked frequently and long in comparison with other users (63.2% of the subjects, p = 0.0029), just like the symptoms of fatigue (45%, p =0.013). Also, the feeling of warmth around the ear and directly to the auricle was reported significantly more frequently by the intensive mobile phone users, compared with other mobile phone users (47.3%, p = 0.00004 vs. 44.6%, p = 0.00063, respectively).Most symptoms appeared during or immediately after a call and disappeared within 2 h after the call. Continuous headache, persisting for longer than 6 h since the end of a call, was reported by 26% of the subjects. **CONCLUSIONS:** Our results show that the mobile phone users may experience subjective symptoms, the intensity of which depends on the intensity of use of mobile phones.

### Szyjkowska A, Bortkiewicz A, Szymczak W, Makowiec-Dabrowska T. [Subjective symptoms related to mobile phone use--a pilot study] Pol Merkuriusz Lek. 19(112):529-532, 2005. [Article in Polish]

Research findings indicate that the use of mobile phones may lead to a number of symptoms such as headache, impaired concentration and memory, fatigue. In Poland this problem has not as yet been addressed by scientific studies. THE AIM: The present project was undertaken to investigate whether the symptoms of ill health reported by young people may be associated with the use of mobile phone. MATERIAL AND METHODS: A survey using a self-reported questionnaire was conducted among randomly selected university students in Lodz, Central Poland. The questionnaire was designed specifically for this study and contained items on health condition and complaints as well as on frequency of mobile phone use. The number of questionnaires necessary for the study was assessed using the simple random sample method. Out of the 160 copies distributed among the students, 140 (87.5%) were completed. Eventually, 117 questionnaires were subject to analysis; the data from respondents who

reported health problems (neck trauma in a car accident, chronic sinusitis and arterial hypertension) were excluded. The following statistical methods were used to analyse questionnaire data: t-Student test for equal and unequal variances or F-Snedecor test for comparing parameters in two study groups, Fisher exact test for comparing frequency, and single and multiple logistic regression models for quantitative risk assessment of negative health outcomes in relation to exposure level and with control for confounders. The subjects were 61 (52.1%) males and 56 females (47.9%). RESULTS: Most of the subjects (62%) assessed their health condition as good, 31% as very good and 7% as fair. 70% complained of headache and 20% of dizziness. Impaired concentration occurred in 56% of respondents. Facial dermatitis was reported by 11%. The most prevalent symptom related to mobile phone use was the thermal sensation within the auricle and behind/around the ear. This was reported by 33 subjects (28.2%). Out of 82 subjects who complained of headache, only 8 (6.8%) related this symptom to mobile phone use. Only 10 subjects of 65 reporting impaired concentration thought it could be associated with their using a mobile phone. The symptoms and health complaints reported by the respondents in no case were the reason for a medical checkup or taking any medication. CONCLUSIONS: The large number of young people complaining of headache and impaired concentration calls for further research to investigate the underlying reasons. It cannot be excluded that one of them may be exposure to EMF emitted by mobile phone. The explanation should be sought through further experimental and epidemiologic studies.

Santini R, Seigne M, Bonhomme-Faivre L, Bouffet S, Defrasne E, Sage M. Symptoms experienced by users of digital cellular phones: a pilot study in a French engineering school. Pathol Biol (Paris) 49(3):222-226, 2001. [Article in French] A survey study, using questionnaire, was conducted in 161 students and workers in a French engineering school on symptoms experienced during use of digital cellular phones. <u>A significant increase in concentration difficult (p < 0.05) was reported by users</u> of 1800-MHz (DCS) cellular phones compared to 900-MHz (GSM) phone users. In users of cellular phones, women significantly (p < 0.05) complained more often of sleep disturbance than men. This sex difference for sleep complaint is not observed between women and men non-users of cellular phone. The use of both cellular phones and VDT significantly (p  $\ddot{A}$  0.05) increased concentration difficulty. Digital cellular phone users also significantly (p < 0.05) more often complained of discomfort, warmth, and picking on the ear during phone conversation in relation with calling duration per day and number of calls per day. The complaint warmth on the ear might be a signal to users for stopping the call.

# Sandstrom M, Wilen J, Oftedal G, Hansson Mild K, Mobile phone use and subjective symptoms. Comparison of symptoms experienced by users of analogue and digital mobile phones. *Occup Med (Lond)* 51(1):25-35, 2001.

In 1995 many people reported symptoms such as headaches, feelings of discomfort, warmth behind/around or on the ear and difficulties concentrating while using mobile phones. The number of complaints was higher for people using the digital (GSM)

system, i.e. with pulse modulated fields, than for those using the analogue (NMT) system. Our main hypothesis was that GSM users experience more symptoms than NMT users. An epidemiological investigation was initiated including 6379 GSM users and 5613 NMT 900 users in Sweden, and 2500 from each category in Norway. The adjusted odds ratio did not indicate any increased risk for symptoms for GSM users compared with NMT 900 users. Our hypothesis was therefore disproved. <u>However, we observed a statistically significant lower risk for sensations of warmth on the ear for GSM users compared with NMT 900 users. The same trend was seen in Norway for sensations of warmth behind/around the ear and in Sweden for headaches and fatigue. Factors distinguishing the two systems (radio frequency emission, phone temperatures and various ergonomic factors) may be responsible for these results, as well as for a secondary finding: a statistically significant association between calling time/number of calls per day and the prevalence of warmth behind/around or on the ear, headaches and fatigue.</u>

Rubin GJ, Cleare AJ, Wessely S. Psychological factors associated with self-reported sensitivity to mobile phones. J Psychosom Res. 64(1):1-9; discussion 11-12, 2008 OBJECTIVE: Some people report symptoms associated with mobile phone use. A minority also report "electrosensitivity," experiencing symptoms following exposure to other electrical devices. Research suggests that electromagnetic fields do not trigger these symptoms. In this study, we examined the differences between these two "sensitive" groups and healthy controls. METHODS: Fifty-two people who reported sensitivity to mobile phones, 19 people who reported sensitivity to mobile phones and "electrosensitivity," and 60 nonsensitive controls completed a questionnaire assessing the following: primary reason for using a mobile phone, psychological health, symptoms of depression, modern health worries (MHW), general health status, symptom severity, and the presence of other medically unexplained syndromes. RESULTS: Perceived sensitivity was associated with an increased likelihood of using a mobile phone predominantly for work (3% of controls, 13% of those sensitive to mobile phones, and 21% of those reporting "electrosensitivity") and greater MHW concerning radiation [mean (S.D.) on a scale of 1-5: 2.0 (1.0), 2.7 (0.9), and 4.0 (0.8), respectively]. Participants who reported "electrosensitivity" also experienced greater depression, greater worries about tainted food and toxic interventions, worse general health on almost every measure, and a greater number of other medically unexplained syndromes compared to participants from the other two groups. No group differences were observed with regards to psychiatric cases. CONCLUSIONS: The data illustrate that patients reporting "electrosensitivity" experience substantially worse health than either healthy individuals or people who report sensitivity to mobile phones but who do not adopt the label "electrosensitivity." Clinicians and researchers would be wise to pay greater attention to this subdivision.

## Oftedal G, Wilen J, Sandstrom M, Mild KH, Symptoms experienced in connection with mobile phone use. *Occup Med (Lond)* 50(4):237-245, 2000.

Many people in Norway and Sweden reported headaches, fatigue, and other symptoms experienced in connection with the use of a mobile phone (MP). Therefore, we initiated

a cross-sectional epidemiological study among 17,000 people, all using an MP in their job. Thirty-one percent of the respondents in Norway and 13% of those in Sweden had experienced at least one symptom in connection with MP use. <u>Next to the sensations of</u> warmth on the ear and behind/around the ear, burning sensations in the facial skin and <u>headaches were most commonly reported</u>. <u>Most symptoms usually began during or</u> within half an hour after the call and lasted for up to 2 h. Relatively few had consulted a physician or been on sick leave because of the symptoms, but about 45% among those with an MP attributed symptom had taken steps to reduce the symptom. <u>These results</u> <u>suggest an awareness of the symptoms</u>, but not necessarily a serious health problem.

#### <u>Khan MM</u>. Adverse effects of excessive mobile phone use.<u>Int J Occup Med Environ</u> <u>Health.</u> 21(4):289-293, 2008.

Introduction: Research findings indicate that the use of mobile phones may lead to a number of symptoms such as headache, impaired concentration and memory, and also fatigue. Materials and Methods: The present study was designed to investigate whether the symptoms of ill health reported by young people may be associated with the use of mobile phone (MP) and to analyze its influence on health and development of medical students. The questionnaire was designed specifically for this study and contained items regarding health condition and health complaints as well as the frequency of MP use. The response rate was 86.6% (286 of 330 forms, completed by 73.77% males and 26.22% females). Results: Most of the subjects (83.57%) had some knowledge about the adverse effects of MP use. 76.92% of the students carried one mobile, and 23.08% more than one. 55.94%, of the subjects reported the average daily MP use of less than 30 min, 27.97%, of 30-60 min, 11.53%, of 60-90 min and 4.54% of more than 90 min. 16.08% of the subjects complained of headache and 24.48% of fatigue. Impaired concentration was reported by 34.27% of respondents, memory disturbances by 40.56%, sleeplessness by 38.8%, hearing problems by 23.07%, and facial dermatitis by 16.78%. The sensation of warmth within the auricle and behind/around the ear was reported by 28.32%. Out of 286 subjects who participated in this study, 44.4% related their symptoms to mobile phone use. Conclusions: The findings of the present study indicate that mobile phones play a large part in the daily life of medical students. Therefore, its impact on psychology and health should be discussed among the students to prevent the harmful effects of mobile phone use.

### <u>Thomée S</u>, <u>Härenstam A</u>, <u>Hagberg M</u>. Mobile phone use and stress, sleep disturbances, and symptoms of depression among young adults--a prospective cohort study.<u>BMC</u> <u>Public Health.</u> 11:66, 2011.

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 1year 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.

# Ikeda K, Nakamura K. Association between mobile phone use and depressed mood in Japanese adolescents: a cross-sectional study. Environ Health Prev Med. 2013 Dec 18. [Epub ahead of print]

OBJECTIVES: Mobile phones are commonly used by adolescents. The aim of this study was to clarify associations between duration of mobile phone use and psychological mood in high school students. METHODS: This cross-sectional study included 2,785 high school students in Niigata, Japan. A self-administered questionnaire was used to elicit information on sex, school year, hours of mobile phone use, psychological mood status, and possible confounders. Psychological mood outcomes were evaluated with the Mood Inventory, developed and validated in 1994, which includes five subcomponents with total scores ranging from 8 to 32 (higher score indicates stronger feeling): "Tension and excitement," "Refreshing mood," "Fatigue," "Depressed mood," and "Anxious mood." Analysis of covariance with Bonferroni's multiple comparison was used to compare mean values among quartiles of hours of mobile phone use. RESULTS: Among the respondents, mean mobile phone use per week was 24 (median 18) h. Long-duration mobile phone use was associated with female students, no participation in sports club activities, early mobile phone use, and fewer hours spent sleeping (all P < 0.001). Overall associations between hours of **mobile phone** use and total scores were significant for "Depressed mood" (P for trend = 0.005), "Tension and excitement" (P for trend <0.001), and "Fatigue" (P for trend < 0.001). Total scores for "Depressed mood," "Tension and excitement," and "Fatigue" of the fourth quartile (≥33 h/week) of mobile phone use were significantly higher than for other quartiles (all P < 0.05). CONCLUSIONS: Increased duration of **mobile phone** use is associated with

unfavorable psychological mood, in particular, a depressed mood. Decreasing mobile phone use may help maintain appropriate mental health in very long-duration users.

## Hocking, B, Preliminary report: symptoms associated with mobile phone use. Occup Med (Lond);48(6):357-360, 1998.

Mobile phone use is ubiquitous, although the alleged health effects of low level radiofrequency radiation (RFR) used in transmission are contentious. Following isolated reports of headache-like symptoms arising in some users, a survey has been conducted to characterize the symptoms sometimes associated with mobile phone usage. A notice of interest in cases was placed in a major medical journal and this was publicized by the media. Respondents were interviewed by telephone using a structured questionnaire. Forty respondents from diverse occupations described unpleasant sensations such as a burning feeling or a dull ache mainly occurring in the temporal, occipital or auricular areas. The symptoms often began minutes after beginning a call, but could come on later during the day. The symptoms usually ceased within an hour after the call, but could last until evening. Symptoms did not occur when using an ordinary handset, and were different from ordinary headaches. There were several reports suggestive of intracranial effects. Three respondents reported local symptoms associated with wearing their mobile phone on their belts. There was one cluster of cases in a workplace. Seventy-five per cent of cases were associated with digital mobile phones. Most of the respondents obtained relief by altering their patterns of telephone usage or type of phone. Cranial and other diverse symptoms may arise associated with mobile phone usage. Physicians and users alike should be alert to this. Further work is needed to determine the range of effects, their mechanism and the possible implications for safety limits of RFR.

### Hocking B, Microwave sickness: a reappraisal. Occup Med (Lond) 51(1):66-69, 2001.

Microwave sickness (MWS) has been a disputed condition. The syndrome involves the nervous system and includes fatigue, headaches, dysaesthesia and various autonomic effects in radiofrequency radiation workers. This paper describes the early reports of the syndrome from Eastern Europe and notes the scepticism expressed about them in the West, before considering comprehensive recent reports by Western specialists and a possible neurological basis for the condition. It is concluded that MWS is a medical entity which should be recognized as a possible risk for radiofrequency radiation workers.

## Hocking B. Management of radiofrequency radiation overexposures. Aust Fam Physician 30(4):339-342, 2001.

BACKGROUND: Radiofrequency radiation (RFR) has been in use for some time but is now proliferative with the burgeoning radiocommunications industry. OBJECTIVE: To inform the profession of the possible health effects from overexposure to radiofrequency radiation (RFR) and the clinical approach to cases. An introduction to the health effects of overexposure to RFR is given. A clinical approach to integrating the patient's symptoms and the circumstances of the exposure is given. Emergency treatment and

ongoing care is outlined, and sources of expert advice given. <u>CONCLUSION</u>: <u>Overexposure to RFR is a complex injury. Advice is given in this article for emergency</u> care and planning ongoing care.

Hanson Mild, K, Oftedal, G, Sandstrom, M, Wilen, J, Tynes, T, Haugsdal, B, Hauger E, Comparison of symptoms experienced by users of analogue and digital mobile phones: a Swedish-Norwegian epidemiological study. Arbetslivsrapport 1998:23. Study of mobile phone users showed a statistically significant association between calling time/number of calls per day and the prevalence of warmth behind/around the ear, headaches, and fatigue.

## Hallberg O. Adverse health indicators correlating with sparsely populated areas in Sweden. Eur J Cancer Prev. 16(1):71-76, 2007.

Earlier studies on health characteristics in Sweden have pointed at a sudden trend change in general health indicators around 1997. The decline was worse in areas with less estimated coverage by the mobile phone system; that is, areas where the average output power from mobile phone handsets is expected to be higher. In this study, health parameters were related to the population density, which is a well defined, rather than an estimated variable. Statistics were obtained from different authorities in Sweden. Data were correlated to the population densities in the 21 different counties of Sweden as well as to estimates of average mobile phone output power. Several health quality measures showed that people in sparsely populated counties in Sweden (as well as in Denmark and Norway) have suffered more illness, and lengthier recovery than people in more densely populated areas since 1997. This is in strong contrast to the situation 20 years ago, when the countryside was the healthiest place in which to live. The indicators strongly correlated with estimated mobile phone area coverage and estimated power output. The indicator statistics suggest that the decline in health in Sweden is not a primary consequence of low population density by itself, but that other factors related to population density are causative. The two factors having the strongest correlation with decreased health quality were the estimated average power output from mobile phones (positive correlation) and the reported coverage from the global system for mobile communication base stations (negative correlation) in each county.

## Hallberg O, Johansson O. Long-term sickness and mobile phone use. J Aust Coll Nutr & Env med 23:11-12, 2004.

The number of people unable to work due to long-term sickness is drastically increasing in Sweden. In this paper we take a close look at the development of mobile phone communication to see how it possibly relates to the health impairment of the Swedish population. Official data was collected regarding mobile phone use and long-term absence from work. The co-variation between those data sets was used to estimate future development of long-term absence rates under the hypothesis that there is a connection between the two sets of data. It was concluded that future long-term absence rates will continue to increase as long as the annual number of ear-heating minute per year is increasing.

# Gómez-Perretta C, Navarro EA, Segura J, Portolés M. Subjective symptoms related to GSM radiation from mobile phone base stations: a cross-sectional study. BMJ Open. 3(12):e003836, 2013. doi: 10.1136/bmjopen-2013-003836.

OBJECTIVES: We performed a re-analysis of the data from Navarro et al (2003) in which health symptoms related to microwave exposure from mobile phone base stations (BSs) were explored, including data obtained in a retrospective inquiry about fear of exposure from BSs. DESIGN: Cross-sectional study. SETTING: La Ñora (Murcia), Spain. PARTICIPANTS: Participants with known illness in 2003 were subsequently disregarded: 88 participants instead of 101 (in 2003) were analysed. Since weather circumstances can influence exposure, we restricted data to measurements made under similar weather conditions. OUTCOMES AND METHODS: A statistical method indifferent to the assumption of normality was employed: namely, binary logistic regression for modelling a binary response (eg, suffering fatigue (1) or not (0)), and so exposure was introduced as a predictor variable. This analysis was carried out on a regular basis and bootstrapping (95% percentile method) was used to provide more accurate CIs. RESULTS: The symptoms most related to exposure were lack of appetite (OR=1.58, 95% CI 1.23 to 2.03); lack of concentration (OR=1.54, 95% CI 1.25 to 1.89); irritability (OR=1.51, 95% CI 1.23 to 1.85); and trouble sleeping (OR=1.49, 95% CI 1.20 to 1.84). Changes in -2 log likelihood showed similar results. Concerns about the BSs were strongly related with trouble sleeping (OR = 3.12, 95% CI 1.10 to 8.86). The exposure variable remained statistically significant in the multivariate analysis. The bootstrapped values were similar to asymptotic CIs. CONCLUSIONS: This study confirms our preliminary results. We observed that the incidence of most of the symptoms was related to exposure levelsindependently of the demographic variables and some possible risk factors. Concerns about adverse effects from exposure, despite being strongly related with sleep disturbances, do not influence the direct association between exposure and sleep.

### <u>Frick U</u>, <u>Rehm J</u>, <u>Eichhammer P</u>. Risk perception, somatization, and self report of complaints related to electromagnetic fields--a randomized survey study.<u>Int J Hyg</u> <u>Environ Health.</u> 205(5):353-360, 2002.

<u>Exposure to electromagnetic</u> fields (EMF) as well as EMF-related complaints has increased over the past decades. However, it is unclear whether these complaints are related to the electromagnetic or other physical properties of these fields per se, to salience of EMF in media, or to both. What is the prevalence of EMF-related complaints in the general population? What are the influencing factors on this prevalence? Does reporting of EMF-related symptoms depend on cognitive factors? To answer these questions, a survey with random variation of three cognitive factors was performed. <u>As</u> <u>expected</u>, EMF-related complaints were reported more by females and people with <u>higher somatization tendency</u>. Age had no significant linear effect on EMF-related complaints. The cognitive condition of threat produced a significant contrast effect among people with high somatization tendency on EMF-related complaints. Cognition can influence reporting of EMF-related effects. Thus, in future research of such effects, psychologically influencing factors should be included. Also risk communication should incorporate knowledge about social cognition.

### Santini R, Santini P, Danze JM, Le Ruz P, Seigne M.Study of the health of people living in the vicinity of mobile phone base stations: I. Influence of distance and sex. Pathol Biol (Paris) 50(6):369-373, 2002. [Article in French]

A survey study using questionnaire was conducted in 530 people (270 men, 260 women) living or not in vicinity of cellular phone base stations, on 18 Non Specific Health Symptoms. Comparisons of complaints frequencies (CHI-SQUARE test with Yates correction) in relation with distance from base station and sex, show significant (p < 0.05) increase as compared to people living > 300 m or not exposed to base station, till 300 m for tiredness, 200 m for headache, sleep disturbance, discomfort, etc. 100 m for irritability, depression, loss of memory, dizziness, libido decrease, etc. Women significantly more often than men (p < 0.05) complained of headache, nausea, loss of appetite, sleep disturbance, depression, discomfort and visual perturbations. This first study on symptoms experienced by people living in vicinity of base stations shows that, in view of radioprotection, minimal distance of people from cellular phone base stations should not be < 300 m.

## Santini R, Santini P, Le Ruz P, Danze JM, Seigne M, Survey study of people living in the vicinity of cellular phone base stations. Electromag Biol Med 22:41-49, 2003.

A survey study was conducted, using a questionnaire, on 530 people (270 men, 260 women) living or not in proximity to cellular phone base stations. Eighteen different symptoms (Non Specific Health Symptoms-NSHS), described as radiofrequency sickness, were studied by means of the chi-square test with Yates correction. The results that were obtained underline that certain complaints are experienced only in the immediate vicinity of base stations (up to 10 m for nausea, loss of appetite, visual disturbances), and other at greater distances from base stations (up to 100 m for irritability, depressive tendencies, lowering of libido, and up to 200 m for headaches, sleep disturbance, feeling of discomfort). In the 200 m to 300 m zone, only the complaint of fatigue is experienced significantly more often when compared with subjects residing at more than 300 m or not exposed (reference group). For seven of the studied symptoms and for the distance up to 300 m, the frequency of reported complaints is significantly higher (P< 0.05) for women in comparison to men. Significant differences are also observed in relation to the ages of subjects, and for the location of subjects in relation to the antennas and to other electromagnetic factors.

Navarro EA, Sequra J, Portoles M, Gomez-Perretta de Mateo C. The Microwave Syndrome: A Preliminary Study in Spain. Electromag Biol Med 22:161-169, 2003. A health survey was carried out in Murcia, Spain, in the vicinity of a Cellular Phone Base Station working in DCS-1800 MHz. This survey contained health items related to "microwave sickness" or "RF syndrome." The microwave power density was measured at the respondents' homes. <u>Statistical analysis showed significant correlation between</u> the declared severity of the symptoms and the measured power density. The separation of respondents into two different exposure groups also showed an increase of the declared severity in the group with the higher exposure.

# <u>Lerchl A</u>, <u>Krüger H</u>, <u>Niehaus M</u>, <u>Streckert JR</u>, <u>Bitz AK</u>, <u>Hansen V</u>. Effects of mobile phone electromagnetic fields at nonthermal SAR values on melatonin and body weight of Djungarian hamsters (Phodopus sungorus). J Pineal Res. 44(3):267-272, 2008.

In three experiments, adult male Djungarian hamsters (Phodopus sungorus) were exposed 24 hr/day for 60 days to radio frequency electromagnetic fields (RF-EMF) at 383, 900, and 1800 MHz, modulated according to the TETRA (383 MHz) and GSM standards (900 and 1800 MHz), respectively. A radial waveguide system ensured a well defined and uniform exposure at whole-body averaged specific absorption rates of 80 mW/kg, which is equal to the upper limit of whole-body exposure of the general population in Germany and other countries. For each experiment, using two identical waveguides, hamsters were exposed (n = 120) and sham-exposed (n = 120) in a blind fashion. In all experiments, pineal and serum melatonin levels as well as the weights of testes, brain, kidneys, and liver were not affected. At 383 MHz, exposure resulted in a significant transient increase in body weight up to 4%, while at 900 MHz this body weight increase was more pronounced (up to 6%) and not transient. At 1800 MHz, no effect on body weight was seen. The results corroborate earlier findings which have shown no effects of RF-EMF on melatonin levels in vivo and in vitro. The data are in accordance with the hypothesis that absorbed RF energy may result in metabolic changes which eventually cause body weight increases in exposed animals. The data support the notion that metabolic effects of RF-EMFs need to be investigated in more detail in future studies.

## <u>Kato Y</u>, <u>Johansson O</u>. Reported functional impairments of electrohypersensitive Japanese: A questionnaire survey. <u>Pathophysiology.</u>19(2) 95-100, 2012.

An increasing number of people worldwide complain that they have become electromagnetic hypersensitive (EHS). We conducted a questionnaire survey of EHS persons in Japan. The aim was to identify electromagnetic fields (EMF) and plausible EMF sources that caused their symptoms. Postal questionnaires were distributed via a self-help group, and 75 participants (95% women) responded. Reported major complaints were "fatigue/tiredness" (85%), "headache", "concentration, memory, and thinking" difficulty (81%, respectively). Seventy-two per cent used some form of complementary/alternative therapy. The most plausible trigger of EHS onset was a mobile phone base station or personal handy-phone system (37%). Sixty-five percent experienced health problems to be due to the radiation from other passengers' mobile phones in trains or buses, and 12% reported that they could not use public transportation at all. Fifty-three percent had a job before the onset, but most had lost their work and/or experienced a decrease in income. Moreover, 85.3% had to take measures to protect themselves from EMF, such as moving to low EMF areas, or buying low EMF electric appliances. EHS persons were suffering not only from their symptoms, but also from economical and social problems.

<u>Hutter HP</u>, <u>Moshammer H</u>, <u>Wallner P</u>, <u>Kundi M</u>. Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations. <u>Occup Environ Med.</u> 63(5):307-313, 2006.

BACKGROUND: The erection of mobile telephone base stations in inhabited areas has raised concerns about possible health effects caused by emitted microwaves. METHODS: In a cross-sectional study of randomly selected inhabitants living in urban and rural areas for more than one year near to 10 selected base stations, 365 subjects were investigated. Several cognitive tests were performed, and wellbeing and sleep quality were assessed. Field strength of high-frequency electromagnetic fields (HF-EMF) was measured in the bedrooms of 336 households. RESULTS: Total HF-EMF and exposure related to mobile telecommunication were far below recommended levels (max. 4.1 mW/m2). Distance from antennae was 24-600 m in the rural area and 20-250 m in the urban area. Average power density was slightly higher in the rural area (0.05 mW/m2) than in the urban area (0.02 mW/m2). Despite the influence of confounding variables, including fear of adverse effects from exposure to HF-EMF from the base station, there was a significant relation of some symptoms to measured power density; this was highest for headaches. Perceptual speed increased, while accuracy decreased insignificantly with increasing exposure levels. There was no significant effect on sleep quality. CONCLUSION: Despite very low exposure to HF-EMF, effects on wellbeing and performance cannot be ruled out, as shown by recently obtained experimental results; however, mechanisms of action at these low levels are unknown.

#### Bortkiewicz A, Zmyslony M, Szyjkowska A, Gadzicka E. [Subjective symptoms reported by people living in the vicinity of cellular phone base stations: a review of the studies] Med Pr. 55(4):345-351, 2004. [Article in Polish]

The problem of health effects of electromagnetic fields (EMF) emitted by cellular phone base stations evokes much interest in view of the fact that people living in their vicinity are fated to continuous exposure to EMF. None of the studies carried out throughout the world have revealed excessive values of standards adopted by the International Commission on Non-Ionizing Radiation Protection (ICNIRP). A questionnaire was used as a study tool. <u>The results of the questionnaire survey reveal that people living in the</u> vicinity of base stations report various complaints mostly of the circulatory system, but also of sleep disturbances, irritability, depression, blurred vision, concentration difficulties, nausea, lack of appetite, headache and vertigo. The performed studies showed the relationship between the incidence of individual symptoms, the level of exposure, and the distance between a residential area and a base station. This association was observed in both groups of persons, those who linked their complaints with the presence of the base station and those who did not notice such a relation. Further studies, clinical and those based on questionnaires, are needed to explain the background of reported complaints.

#### <u>Bortkiewicz A, Gadzicka E, Szyjkowska A, Politański P, Mamrot P, Szymczak W,</u> <u>Zmyślony M</u>. Subjective complaints of people living near mobile phone base stations

in Poland. Int J Occup Med Environ Health. 25(1):31-40, 2012.

OBJECTIVES: The aim of our study was to assess the health conditions and subjective symptoms of the inhabitants living in the base stations vicinity and to analyse the relationship between the complaints and level of exposure to electromagnetic fields

(EMF).MATERIALS AND METHODS: Our study was performed in housing estates located in five regions of Łódź. The electric field measurements were performed in the buildings located closest to the azimuth of the antennas. Respondents were selected by trained interviewers using an uniform procedure. The number of the households to be examined was set at a minimum of 420. The guestionnaire contained: demographic data, occupational and environmental exposure to EMF, health condition, subjective complaints. Results were adjusted for confounders (age, gender, EMF at the workplace and EMF emitted by household equipment) using multiple regression model.RESULTS: 181 men and 319 women from 500 households were examined. Electric field above 0.8 V/m was recorded in 12% of flats. There was no significant correlation between electric field strength and the distance of examined flats from the base stations. To make possible comparison with relevant literature, we analysed also the frequency of the reported symptoms vs. the distance. Headache was declared by 57% people, most frequently (36.4%) living 100-150 m away from the base station compared to people living at longer distances (p = 0.013). 24.4% subjects, mostly living at a distance above 150 m, declared impaired memory. Difference was statistically significant in comparison with people living at other distances (p = 0.004).CONCLUSIONS: The explanation why we did not find any correlation between the electric field strength and frequency of subjective symptoms but found a correlation between subjective symptoms and distance from base station needs further studies. Maybe new metrics of exposure assessment should be adopted for this purpose.

## <u>Augner C</u>, <u>Florian M</u>, <u>Pauser G</u>, <u>Oberfeld G</u>, <u>Hacker GW</u>. GSM base stations: Short-term effects on well-being. <u>Bioelectromagnetics.</u> 30:73-80, 2009.

The purpose of this study was to examine the effects of short-term GSM (Global System for Mobile Communications) cellular phone base station RF-EMF (radiofrequency electromagnetic fields) exposure on psychological symptoms (good mood, alertness, calmness) as measured by a standardized well-being questionnaire. Fifty-seven participants were selected and randomly assigned to one of three different exposure scenarios. Each of those scenarios subjected participants to five 50-min exposure sessions, with only the first four relevant for the study of psychological symptoms. Three exposure levels were created by shielding devices in a field laboratory, which could be installed or removed during the breaks between sessions such that double-blinded conditions prevailed. The overall median power flux densities were 5.2 microW/m(2) during "low," 153.6 microW/m(2) during "medium," and 2126.8 microW/m(2) during "high" exposure sessions. For scenario HM and MH, the first and third sessions were "low" exposure. The second session was "high" and the fourth was "medium" in scenario HM; and vice versa for scenario MH. Scenario LL had four successive "low" exposure sessions constituting the reference condition. Participants in scenarios HM and MH (high and medium exposure) were significantly calmer during those sessions than participants in scenario LL (low exposure throughout) (P = 0.042). However, no significant differences between exposure scenarios in the "good mood" or "alertness" factors were obtained. We conclude that short-term exposure to GSM base station signals may have an impact on well-being by reducing psychological arousal.

Augner C, Hacker GW. Are people living next to mobile phone base stations more strained? Relationship of health concerns, self-estimated distance to base station, and psychological parameters. Indian J Occup Environ Med. 13(3):141-145, 2009.

BACKGROUND AND AIMS: Coeval with the expansion of mobile phone technology and the associated obvious presence of mobile phone base stations, some people living close to these masts reported symptoms they attributed to electromagnetic fields (EMF). Public and scientific discussions arose with regard to whether these symptoms were due to EMF or were nocebo effects. The aim of this study was to find out if people who believe that they live close to base stations show psychological or psychobiological differences that would indicate more strain or stress. Furthermore, we wanted to detect the relevant connections linking self-estimated distance between home and the next mobile phone base station (DBS), daily use of mobile phone (MPU), EMF-health concerns, electromagnetic hypersensitivity, and psychological strain parameters. DESIGN, MATERIALS AND METHODS: Fifty-seven participants completed standardized and non-standardized questionnaires that focused on the relevant parameters. In addition, saliva samples were used as an indication to determine the psychobiological strain by concentration of alpha-amylase, cortisol, immunoglobulin A (IgA), and substance P. RESULTS: Self-declared base station neighbors (DBS </= 100 meters) had significantly higher concentrations of alpha-amylase in their saliva, higher rates in symptom checklist subscales (SCL) somatization, obsessive-compulsive, anxiety, phobic anxiety, and global strain index PST (Positive Symptom Total). There were no differences in EMF-related health concern scales. CONCLUSIONS: We conclude that self-declared base station neighbors are more strained than others. EMF-related health concerns cannot explain these findings. Further research should identify if actual EMF exposure or other factors are responsible for these results.

#### <u>Blettner M</u>, <u>Schlehofer B</u>, <u>Breckenkamp J</u>, <u>Kowall B</u>, <u>Schmiedel S</u>, <u>Reis U</u>, <u>Potthoff P</u>, <u>Schuez J</u>, <u>Berg-Beckhoff G</u>. Mobile phone base stations and adverse health effects: Phase 1: A population-based cross-sectional study in Germany. <u>Occup Environ Med</u>. 66(2):118-123. 2009.

Abstract OBJECTIVE: The aim of this first phase of a cross-sectional study from Germany was to investigate whether proximity of residence to mobile phone base stations as well as risk perception is associated with health complaints. METHODS: We conducted a population-based multi-phase cross-sectional study within the context of a large panel survey regularly carried out by a private research institute in Germany. In the initial phase, which we will report on in this paper, 30,047 persons from a total of 51,444 who took part in the nationwide survey also answered questions on how mobile phone base stations affect their health. A list of 38 health complaints was used. A multiple linear regression model was used to identify predictors of health complaints including proximity of residence to mobile phone base stations and risk perception. <u>RESULTS: Of the 30,047 participants (response rate 58.6%), 18.7% of participants were concerned about adverse health effects of mobile phone base stations, while an additional 10.3% attributed their personal adverse health effects to the exposure from them. Participants who are concerned about or attribute adverse health effects to mobile phone base</u>

stations and those living in the vicinity of a mobile phone base station (500 m) reported slightly more health complaints than others. CONCLUSIONS: A substantial proportion of the German population is concerned about adverse health effects caused by exposure from mobile phone base stations. The observed slightly higher prevalence of health complaints near base stations can however not be fully explained by attributions or concerns.

### <u>Kowall B</u>, <u>Breckenkamp J</u>, <u>Heyer K</u>, <u>Berg-Beckhoff G</u>. German wide cross sectional survey on health impacts of electromagnetic fields in the view of general practitioners. Int J Public Health.55(5):507-512, 2010.

OBJECTIVES: The proportion of **general practitioners (GPs)** in Germany who assume health impacts of electromagnetic fields (EMF) is assessed. Moreover, factors associated with this risk perception are examined. METHODS: A 7% random sample was drawn from online lists of all the GPs working in Germany. 1,867 doctors received a long version of a self-administered postal questionnaire about EMF and health (response rate 23.3%), 928 doctors received a short version (response rate 49.1%). RESULTS: 37.3% of responders to the short and 57.5% of responders to the long questionnaire agreed "that there are persons whose health complaints are caused by EMF when legal limit values are met". A late responder analysis for the survey with the short questionnaire led to a still lower estimate of 29% for GPs believing in health-relevant effects of EMF. <u>CONCLUSION: About a third of German GPs associate EMF with health complaints and thus deviate considerably from current scientific knowledge.</u> To avoid a strong selection bias in the surveys of the perception of EMF risks, use of short questionnaires and late responder analysis are recommended.

Kato Y, Johansson O. Reported functional impairments of electrohypersensitive Japanese: A questionnaire survey. Pathophysiology.19(2) 95-100, 2012. An increasing number of people worldwide complain that they have become electromagnetic hypersensitive (EHS). We conducted a questionnaire survey of EHS persons in Japan. The aim was to identify electromagnetic fields (EMF) and plausible EMF sources that caused their symptoms. Postal guestionnaires were distributed via a self-help group, and 75 participants (95% women) responded. Reported major complaints were "fatigue/tiredness" (85%), "headache", "concentration, memory, and thinking" difficulty (81%, respectively). Seventy-two per cent used some form of complementary/alternative therapy. The most plausible trigger of EHS onset was a mobile phone base station or personal handy-phone system (37%). Sixty-five percent experienced health problems to be due to the radiation from other passengers' mobile phones in trains or buses, and 12% reported that they could not use public transportation at all. Fifty-three percent had a job before the onset, but most had lost their work and/or experienced a decrease in income. Moreover, 85.3% had to take measures to protect themselves from EMF, such as moving to low EMF areas, or buying low EMF electric appliances. EHS persons were suffering not only from their symptoms, but also from economical and social problems.

# <u>Bergdahl J</u>, <u>Tillberg A</u>, <u>Stenman E</u>. Odontologic survey of referred patients with symptoms allegedly caused by electricity or visual display units. <u>Acta Odontol Scand</u>. 56(5):303-307, 1998.

Twenty-eight consecutive patients with symptoms allegedly caused by electricity or visual display units were odontologically investigated according to a specially designed registration form including an anamnestic interview and a clinical protocol. The most common oral and general symptoms reported were burning mouth, craniomandibular dysfunction symptoms, skin complaints, and fatigue. Oral symptoms such as craniomandibular dysfunction and general symptoms such as eye complaints and dizziness scored highest on a visual analog scale regarding mean symptom intensity. The patients reported various numbers of medical diagnoses, such as allergic rhinitis or asthma and hypothyroidism. Various dental diseases were found; the most common were temporomandibular joint and masticatory muscle dysfunctions, lesions in the oral mucosa, and periodontal diseases. Urinary-Hg (U-Hg) analysis showed a mean U-Hg concentration of 8.5 nmol Hg/L urine, and none of the patients exceeded the limit of 50 nmol Hg/L urine. The U-Hg concentration was positively correlated with the number of amalgam fillings (P< 0.01) and craniomandibular disorders (P < 0.05). No or low secretion of the minor mucous glands was found in 43% of the patients. One patient showed hypersensitivity to gold and cobalt. The present study showed that various odontologic factors might be involved in some of these patients' suffering. Thus, it is important that professionals from other disciplines collaborate with dentistry if these patients are to be properly investigated.

### **Effects on Sleep**

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

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) ( $\leq$  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'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.

# 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.

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. <u>The</u> <u>latency of REM sleep increased due to radiation exposure indicating a change in the</u> <u>ultradian rhythm of normal sleep cycles. The cumulative and irreversible effect of</u> <u>radiation exposure was proposed and the interaction of the extremely low frequency</u> <u>radiation with the similar EEG frequencies was suggested.</u>

## Mann, K, Roschke, J, Effects of pulsed high-frequency electromagnetic fields on human sleep. Neuropsychobiology 33(1):41-47, 1996.

In the present study we investigated the influence of pulsed high-frequency electromagnetic fields of digital mobile radio telephones on sleep in healthy humans. <u>Besides a hypnotic effect with shortening of sleep onset latency, a REM suppressive</u> <u>effect with reduction of duration and percentage of REM sleep was found. Moreover,</u> <u>spectral analysis revealed qualitative alterations of the EEG signal during REM sleep with</u> <u>an increased spectral power density. Knowing the relevance of REM sleep for adequate</u> <u>information processing in the brain, especially concerning mnestic functions and</u> <u>learning processes, the results emphasize the necessity to carry out further</u> <u>investigations on the interaction of this type of electromagnetic fields and the human</u> <u>organism.</u>

### Lustenberger C, Murbach M, Dürr 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. 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 affect cortical activity during sleep and to test whether such effects on cortical activity during sleep interact with sleepdependent 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). <u>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.</u>

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

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. Fortyeight 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.

## 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.

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 <u>"virtual" spatial navigation task</u> 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. <u>Results revealed a main effect of RF exposure and a significant RF exposure by group effect on distance traveled during the trials.</u> 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.

# 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.

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.

# <u>Loughran SP</u>, <u>Wood AW</u>, <u>Barton JM</u>, <u>Croft RJ</u>, <u>Thompson B</u>, <u>Stough C</u>. The effect of electromagnetic fields emitted by mobile phones on human sleep. Neuroreport. 16(17):1973-1976, 2005.

Previous research has suggested that exposure to radiofrequency electromagnetic fields increases electroencephalogram spectral power in non-rapid eye movement sleep. Other sleep parameters have also been affected following exposure. We examined whether aspects of sleep architecture show sensitivity to electromagnetic fields emitted by digital mobile phone handsets. Fifty participants were exposed to electromagnetic

fields for 30 min prior to sleep. Results showed a decrease in rapid eye movement sleep latency and increased electroencephalogram spectral power in the 11.5-12.25 Hz frequency range during the initial part of sleep following exposure. <u>These results are</u> <u>evidence that mobile phone exposure prior to sleep may promote rapid eye movement</u> <u>sleep and modify the sleep electroencephalogram in the first non-rapid eye movement</u> <u>sleep period.</u>

### Liu H, Chen G, Pan Y, Chen Z, Jin W, Sun C, Chen C, Dong X, Chen K, Xu Z, Zhang S, Yu Y. (2014) Occupational Electromagnetic Field Exposures Associated with Sleep Quality: A Cross-Sectional Study. PLoS ONE 9(10): e110825. doi:10.1371/journal.pone.0110825.

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

# Lebedeva NN, Sulimov AV, Sulimova OP, Korotkovskaya TI, Gailus T, Investigation of brain potentials in sleeping humans exposed to the electromagnetic field of mobile phones. Crit Rev Biomed Eng 29(1):125-133, 2001.

An investigation was made of 8-hour EEG tracings of sleeping humans exposed to the electromagnetic field of a GSM-standard mobile phone. To analyze the EEG-patterns, manual scoring, nonlinear dynamics, and spectral analysis were employed. It was found that, when human beings were exposed to the electromagnetic field of a cellular phone, their cerebral cortex biopotentials revealed an increase in the alpha-range power density as compared to the placebo experiment. It was also found that the dimension of EEG correlation dynamics and the relation of sleep stages changed under the influence

of the electromagnetic field of a mobile phone.

Huber R, Graf T, Cote KA, Wittmann L, Gallmann E, Matter D, Schuderer J, Kuster N, Borbely AA, Achermann P, Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG. *Neuroreport* 11(15):3321-3325, 2000. The aim of the study was to investigate whether the electromagnetic field (EMF) emitted by digital radiotelephone handsets affects brain physiology. Healthy, young male subjects were exposed for 30 min to EMF (900 MHz; spatial peak specific absorption rate 1 W/kg) during the waking period preceding sleep. Compared with the control condition with sham exposure, spectral power of the EEG in non-rapid eye movement sleep was increased. The maximum rise occurred in the 9.75-11.25 Hz and 12.5-13.25 Hz band during the initial part of sleep. These changes correspond to those obtained in a previous study where EMF was intermittently applied during sleep. Unilateral exposure induced no hemispheric asymmetry of EEG power. <u>The present</u> results demonstrate that exposure during waking modifies the EEG during subsequent sleep. Thus the changes of brain function induced by pulsed high-frequency EMF outlast the exposure period.

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

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 pulsemodulated 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.

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. doi: 10.1371/journal.pone.0099007. eCollection 2014.

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  $Ta = 31^{\circ}C$ 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.

#### HuberR, TreyerV, BorbélyAA, SchudererJ, GottseligJM, LandoltH-P, WerthE, BertholdT, KusterN, BuckA, AchermannP, 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.

Usage of mobile phones is rapidly increasing, but there is limited data on the possible effects of electromagnetic field (EMF) exposure on brain physiology. We investigated the effect of EMF vs. sham control exposure on waking regional cerebral blood flow (rCBF) and on waking and sleep electroencephalogram (EEG) in humans. In Experiment 1, positron emission tomography (PET) scans were taken after unilateral head exposure to 30-min pulse-modulated 900 MHz electromagnetic field (pm-EMF). In Experiment 2, night-time sleep was polysomnographically recorded after EMF exposure. Pulse-modulated EMF exposure increased relative rCBF in the dorsolateral prefrontal cortex ipsilateral to exposure. Also, pm-EMF exposure enhanced EEG power in the alpha frequency range prior to sleep onset and in the spindle frequency range during stage 2 sleep. Exposure to EMF without pulse modulation did not enhance power in the waking or sleep EEG. We previously observed EMF effects on the sleep EEG (A. A. Borbély, R. Huber, T. Graf, B. Fuchs, E. Gallmann and P. Achermann. Neurosci. Lett., 1999, 275: 207-210; R. Huber, T. Graf, K. A. Cote, L. Wittmann, E. Gallmann, D. Matter, J. Schuderer, N. Kuster, A. A. Borbély, and P. Achermann. Neuroreport, 2000, 11: 3321-3325), but the

basis for these effects was unknown. <u>The present results show for the first time that (1)</u> pm-EMF alters waking rCBF and (2) pulse modulation of EMF is necessary to induce waking and sleep EEG changes. Pulse-modulated EMF exposure may provide a new, non-invasive method for modifying brain function for experimental, diagnostic and therapeutic purposes.

Huber R, Schuderer J, Graf T, Jutz K, Borbely AA, Kuster N, Achermann P. Radio frequency electromagnetic field exposure in humans: Estimation of SAR distribution in the brain, effects on sleep and heart rate. Bioelectromagnetics 24(4):262-276, 2003. In two previous studies we demonstrated that radiofrequency electromagnetic fields (RF EMF) similar to those emitted by digital radiotelephone handsets affect brain physiology of healthy young subjects exposed to RF EMF (900 MHz; spatial peak specific absorption rate [SAR] 1 W/kg) either during sleep or during the waking period preceding sleep. In the first experiment, subjects were exposed intermittently during an 8 h nighttime sleep episode and in the second experiment, unilaterally for 30 min prior to a 3 h daytime sleep episode. Here we report an extended analysis of the two studies as well as the detailed dosimetry of the brain areas, including the assessment of the exposure variability and uncertainties. The latter enabled a more in depth analysis and discussion of the findings. Compared to the control condition with sham exposure, spectral power of the non-rapid eye movement sleep electroencephalogram (EEG) was initially increased in the 9-14 Hz range in both experiments. No topographical differences with respect to the effect of RF EMF exposure were observed in the two experiments. Even unilateral exposure during waking induced a similar effect in both hemispheres. Exposure during sleep reduced waking after sleep onset and affected heart rate variability. Exposure prior to sleep reduced heart rate during waking and stage 1 sleep. The lack of asymmetries in the effects on sleep EEG, independent of bi- or unilateral exposure of the cortex, may indicate involvement of subcortical bilateral projections to the cortex in the generation of brain function changes, especially since the exposure of the thalamus was similar in both experiments (approx. 0.1 W/kg).

# Huber R, Treyer V, Schuderer J, Berthold T, Buck A, Kuster N, Landolt HP, Achermann P. Exposure to pulse-modulated radio frequency electromagnetic fields affects regional cerebral blood flow. Eur J Neurosci. 21(4):1000-1006, 2005.

We investigated the effects of radio frequency electromagnetic fields (RF EMF) similar to those emitted by mobile phones on waking regional cerebral blood flow (rCBF) in 12 healthy young men. Two types of RF EMF exposure were applied: a 'base-station-like' and a 'handset-like' signal. Positron emission tomography scans were taken after 30 min unilateral head exposure to pulse-modulated 900 MHz RF EMF (10 g tissue-averaged spatial peak-specific absorption rate of 1 W/kg for both conditions) and sham control. We observed an increase in relative rCBF in the dorsolateral prefrontal cortex on the side of exposure. The effect depended on the spectral power in the amplitude modulation of the RF carrier such that only 'handset-like' RF EMF exposure with its stronger low-frequency components but not the 'base-station-like' RF EMF exposure affected rCBF. This finding supports our previous observation that pulse modulation of

<u>RF EMF is necessary to induce changes in the waking and sleep EEG, and substantiates</u> <u>the notion that pulse modulation is crucial for RF EMF-induced alterations in brain</u> <u>physiology.</u>

#### <u>Hung CS</u>, <u>Anderson C</u>, <u>Horne JA</u>, <u>McEvoy P</u>. Mobile phone 'talk-mode' signal delays EEG-determined sleep onset. <u>Neurosci Lett.</u> 421: 82-86, 2007.

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 30min, at 13:30h, 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 3min (before, during and after exposure). After exposure the phone and base-station were switched off, the bedroom darkened, and a 90min 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 guite 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.

# <u>Rusterholz T</u>, <u>Bersagliere A</u>, <u>Kuster N</u>, <u>Achermann P</u>. Sleep EEG alterations: effects of different pulse-modulated radio frequency electromagnetic fields.<u>J Sleep Res.</u> 21(1):50-58, 2012.

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. <u>Consistent with previous findings, our results provide further evidence that pulse-</u> <u>modulated RF EMF alter brain physiology, although the time-course of the effect</u> <u>remains variable across studies. Additionally, we demonstrated that modulation</u> <u>frequency components within a physiological range may be sufficient to induce these</u> <u>effects.</u>

#### Schmid MR, Loughran SP, Regel SJ, Murbach M, Bratic Grunauer A,

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

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.

# 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.

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. <u>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.</u>

### Liu H, Chen G, Pan Y, Chen Z, Jin W, Sun C, Chen C, Dong X, Chen K, Xu Z, Zhang S, Yu Y. (2014) Occupational Electromagnetic Field Exposures Associated with Sleep Quality: A Cross-Sectional Study. PLoS ONE 9(10): e110825. doi:10.1371/journal.pone.0110825.

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

## Hung CS, Anderson C, Horne JA, McEvoy P. Mobile phone 'talk-mode' signal delays EEG-determined sleep onset. <u>Neurosci Lett.</u> 421: 82-86, 2007.

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 30min, at 13:30h, 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 3min (before, during and after exposure). After exposure the phone and base-station were switched off, the bedroom darkened, and a 90min 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. <u>Post-exposure</u>, 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.

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

### **Effects On Pregnancy and the Fetus**

Luo Q, Jiang Y, Jin M, Xu J, Huang HF. Proteomic Analysis on the Alteration of Protein Expression in the Early-Stage Placental Villous Tissue of Electromagnetic Fields Associated With Cell Phone Exposure. Reprod Sci. 2013 Feb 18. [Epub ahead of print] Background: To explore the possible adverse effects and search for cell phone electromagnetic field (EMF)-responsive proteins in human early reproduction, a proteomics approach was employed to investigate the changes in protein expression profile induced by cell phone EMF in human chorionic tissues of early pregnancy in vivo.Methods:Volunteer women about 50 days pregnant were exposed to EMF at the average absorption rate of 1.6 to 8.8 W/kg for 1 hour with the irradiation device placed 10 cm away from the umbilicus at the midline of the abdomen. The changes in protein profile were examined using 2-dimensional electrophoresis (2-DE).Results:Up to 15 spots have yielded significant change at least 2- to 2.5-folds up or down compared to sham-exposed group. Twelve proteins were identified- procollagen-proline, eukaryotic translation elongation factor 1 delta, chain D crystal structure of human vitamin Dbinding protein, thioredoxin-like 3, capping protein, isocitrate dehydrogenase 3 alpha, calumenin, Catechol-O-methyltransferase protein, proteinase inhibitor 6 (PI-6; SerpinB6) protein, 3,2-trans-enoyl-CoA isomerase protein, chain B human erythrocyte 2,3bisphosphoglycerate mutase, and nucleoprotein.Conclusion:Cell phone EMF might alter the protein profile of chorionic tissue of early pregnancy, during the most sensitive stage of the embryos. The exposure to EMF may cause adverse effects on cell proliferation and development of nervous system in early embryos. Furthermore, 2-DE coupled with mass spectrometry is a promising approach to elucidate the effects and search for new biomarkers for environmental toxic effects.

### 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.

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. <u>Our results show that the application of a 900 MHz EMF in the</u> <u>prenatal period adversely affected female pups' learning behavior and also resulted in</u> <u>histopathological changes appearing in the hippocampus</u>.

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. 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, preand 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 ( $\sim 2 \text{ g/kg}$ ). 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.

### <u>Aldad TS</u>, <u>Gan G</u>, <u>Gao XB</u>, <u>Taylor HS</u>. Fetal radiofrequency radiation exposure from 800-1900 mhz-rated cellular telephones affects neurodevelopment and behavior in mice. <u>Sci Rep.</u> 2:312, 2012.

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.

## Barteri M, Pala A, Rotella S. Structural and kinetic effects of mobile phone microwaves on acetylcholinesterase activity. Biophys Chem. 113(3):245-253, 2005.

The present study provides evidence that "in vitro" simple exposure of an aqueous solution of electric eel acetylcholinesterase (EeAChE; EC 3.1.1.7.) to cellular phone emission alters its enzymatic activity. <u>This paper demonstrates, by combining different experimental techniques, that radio frequency (RF) radiations irreversibly affect the structural and biochemical characteristics of an important CNS enzyme. These results were obtained by using a commercial cellular phone to reproduce the reality of the human exposition. This experimental procedure provided surprising effects collected practically without experimental errors because they were obtained comparing native and irradiated sample of the same enzyme solution. Although these results cannot be used to conclude whether exposure to RF during the use of cellular phone can lead to any hazardous health effect, they may be a significant first step towards further verification of these effects on other "ex vivo" or "in vivo" biological systems.</u>

### 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]

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  $\beta$ -carotene concentrations decreased in the EMR groups, although brain iron, vitamin A, and  $\beta$ -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.

# 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.

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 dentate gyrus. Cell loss might be caused by an inhibition of granule cell neurogenesis in the dentate gyrus.

### 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.

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.

## <u>Jing J</u>, <u>Yuhua Z</u>, <u>Xiao-qian Y</u>, <u>Rongping J</u>, <u>Dong-mei G</u>, <u>Xi C</u>. The influence of microwave radiation from cellular phone on fetal rat brain. <u>Electromagn Biol Med.</u> 31(1):57-66,

### 2012.

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.

# 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]

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 cerebellumdependent 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.

Orhan Baş, Osman Fikret Sönmez, Ali Aslan, Ayşe İkinci, Hatice Hancı, Mehmet Yıldırım, Haydar Kaya, Metehan Akça, Ersan Odacı. 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.

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.

#### Ayşe İkinci, Ersan Odacı, Mehmet Yıldırım, Haydar Kaya, Metehan Akça, Hatice Hancı, Ali Aslan, Osman Fikret Sönmez, Orhan Baş.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. December 2013.

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. <u>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.</u>