

**Annotated Bibliography of Scientific Papers
Finding Evidence of Harm from Cell Phone Radiation Exposure
Published between August, 2016 and July, 2018**

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1.0. Review Papers

1.1. Radiofrequency and non-ionizing radiation effects - reviews

Thermal and non-thermal health effects of low intensity non-ionizing radiation: An international perspective

Belpomme D, Hardell, L, Belyaev I, Burgio E, Carpenter DO. Thermal and non-thermal health effects of low intensity non-ionizing radiation: An international perspective. Environ Pollut. 2018 Jul 6;242(Pt A):643-658. doi: 10.1016/j.envpol.2018.07.019.

Highlights

- Exposure to electromagnetic fields has increased dramatically.
- Electromagnetic fields at low and non-thermal intensities increase risk of cancer in animals and humans.
- Some individuals are particularly sensitive and develop a syndrome of electrohypersensitivity.
- There is an urgent need to recognize hazards associated with excessive exposure to non-thermal levels of electromagnetic fields.

Abstract

Exposure to low frequency and radiofrequency electromagnetic fields at low intensities poses a significant health hazard that has not been adequately addressed by national and international organizations such as the World Health Organization. There is strong evidence that excessive exposure to mobile phone-frequencies over long periods of time increases the risk of brain cancer both in humans and animals. The mechanism(s) responsible include induction of reactive oxygen species, gene expression alteration and DNA damage through both epigenetic and genetic processes. In vivo and in vitro studies demonstrate adverse effects on male and female reproduction, almost certainly due to generation of reactive oxygen species. There is increasing evidence the exposures can result in neurobehavioral decrements and that some individuals develop a syndrome of "electro-hypersensitivity" or "microwave illness", which is one of several syndromes commonly categorized as "idiopathic environmental intolerance". While the symptoms are non-specific, new biochemical indicators and imaging techniques allow diagnosis that excludes the symptoms as being only psychosomatic. Unfortunately standards

set by most national and international bodies are not protective of human health. This is a particular concern in children, given the rapid expansion of use of wireless technologies, the greater susceptibility of the developing nervous system, the hyperconductivity of their brain tissue, the greater penetration of radiofrequency radiation relative to head size and their potential for a longer lifetime exposure.

<https://www.ncbi.nlm.nih.gov/pubmed/30025338>

Public Health Implications of Human Exposure to EMFs

The incidence of brain cancer in children and adolescents has increased between 2000 and 2010 (Ostrom et al., 2015). Gliomas are increasing in the Netherlands (Ho et al., 2014), glioblastomas are increasing in Australia (Dobes et al., 2011) and England (Philips et al., 2018) and all brain cancers are increasing in Spain (Etxeberrua et al., 2015) and Sweden (Hardell and Carlberg, 2017). The latency period between initial exposure and clinical occurrence of brain cancer is not known but is estimated to be long. While not all reports of brain cancer rates show an increase, some do. The continually increasing exposure to EMFs from all sources may contribute to these increases. The prevalence of EHS is unknown, but various reports suggest that it is between 1 and 10% of the population (Hallberg and Oberfeld, 2006; Huang et al., 2018). Male fertility has been declining (Geoffroy-Siraudin et al., 2012; Levine et al., 2017). EMFs increase the risk of each of these diseases and others. Alzheimer's disease is increasing in many countries worldwide and its association with ELF-EMF occupational exposure has been clearly demonstrated through several independent epidemiological studies (Davanipour and Sobel, 2009; Sobel et al., 1996; Qiu et al., 2004) and a meta-analysis of these studies (García et al., 2008). A recent meta-analysis (Huss et al., 2018) has reported an increased risk of amyotrophic lateral sclerosis in workers occupationally exposure to ELF-EMFs.

Safety limits for RF exposure have been based (until today) on the thermal effects of EMFs. But these standards do not protect people, particularly children, from the deleterious health effects of non-thermal EMFs (Nazıroğlu et al., 2013; Mahmoudabadi et al., 2015). Each of these diseases is associated with decrements in health and quality of life. Brain cancer patients often die in spite of some improvement in treatment, while EHS patients present with increased levels of distress, inability to work, and progressive social withdrawal. The ability for humans to reproduce is fundamental for the maintenance of our species.

The scientific evidence for harm from EMFs is increasingly strong. We do not advocate going back to the age before electricity or wireless communication, but we deplore the present failure of public health international bodies to recognize the scientific data showing the adverse effects of EMFs on human health. It is encouraging that some governments are taking action. France has removed WiFi from pre-schools and ordered Wi-Fi to be shut off in elementary schools when not in use (<http://www.telegraph.co.uk/news/2017/12/11/france-ipose-total-ban-mobile-phones-schools/>). **The State of California Department of Public Health has issued a warning on use of mobile phones and offered advice on how to reduce exposure (State of California, 2017).** There are many steps that are neither difficult nor expensive that can be taken to use modern technology but in a manner that significantly reduces threats to human

health.

It is urgent that national and international bodies, particularly the WHO, take this significant public health hazard seriously and make appropriate recommendations for protective measures to reduce exposures. This is especially urgently needed for children and adolescents. It is also important that all parts of society, especially the medical community, educators, and the general public, become informed about the hazards associated with exposure to EMFs and of the steps that can be easily taken to reduce exposure and risk of associated disease.

<https://www.ncbi.nlm.nih.gov/pubmed/30025338>

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World Health Organization, radiofrequency radiation and health - a hard nut to crack (Review)

Hardell L. World Health Organization, radiofrequency radiation and health - a hard nut to crack (Review). *Int J Oncol.* 2017 Aug;51(2):405-413. doi: 10.3892/ijo.2017.4046.

Abstract

In May 2011 the International Agency for Research on Cancer (IARC) evaluated cancer risks from radiofrequency (RF) radiation. Human epidemiological studies gave evidence of increased risk for glioma and acoustic neuroma. RF radiation was classified as Group 2B, a possible human carcinogen. Further epidemiological, animal and mechanistic studies have strengthened the association. In spite of this, in most countries little or nothing has been done to reduce exposure and educate people on health hazards from RF radiation. On the contrary ambient levels have increased. In 2014 the WHO launched a draft of a Monograph on RF fields and health for public comments. It turned out that five of the six members of the Core Group in charge of the draft are affiliated with International Commission on Non-Ionizing Radiation Protection (ICNIRP), an industry loyal NGO, and thus have a serious conflict of interest. Just as by ICNIRP, evaluation of non-thermal biological effects from RF radiation are dismissed as scientific evidence of adverse health effects in the Monograph. This has provoked many comments sent to the WHO. However, at a meeting on March 3, 2017 at the WHO Geneva office it was stated that the WHO has no intention to change the Core Group.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5504984/>

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Database of bio-effects from non-ionizing radiation

Leach V, Weller S, Redmayne M. A novel database of bio-effects from non-ionizing radiation. *Rev Environ Health.* 2018 Jun 6. pii: /j/reveh.ahead-of-print/reveh-2018-0017/reveh-2018-0017.xml.

Abstract

A significant amount of electromagnetic field/electromagnetic radiation (EMF/EMR) research is available that examines biological and disease associated endpoints. The quantity, variety and changing parameters in the available research can be challenging when undertaking a literature review, meta-analysis, preparing a study design, building reference lists or comparing findings between relevant scientific papers. The Oceania Radiofrequency Scientific Advisory Association (ORSAA) has created a comprehensive, non-biased, multi-categorized, searchable database of papers on non-ionizing EMF/EMR to help address these challenges. It is regularly added to, freely accessible online and designed to allow data to be easily retrieved, sorted and analyzed. This paper demonstrates the content and search flexibility of the ORSAA database. Demonstration searches are presented by Effect/No Effect; frequency-band/s; in vitro; in vivo; biological effects; study type; and funding source.

As of September 15, 2017, the clear majority of 2653 papers captured in the database examine outcomes in the 300 MHz-3 GHz range. There are 3 times more biological "Effect" than "No Effect" papers; nearly a third of papers provide no funding statement; industry-funded studies more often than not find "No Effect", while institutional funding commonly reveal "Effects". Country of origin where the study is conducted/funded also appears to have a dramatic influence on the likely result outcome.

<https://www.ncbi.nlm.nih.gov/pubmed/29874195>

1.2. Cancer risk -- reviews and meta-analyses

Evaluation of Mobile Phone & Cordless Phone Use & Glioma Risk Using the Bradford Hill Viewpoints from 1965 on Association or Causation

Carlberg M, Hardell L. Evaluation of Mobile Phone and Cordless Phone Use and Glioma Risk Using the Bradford Hill Viewpoints from 1965 on Association or Causation. *Biomed Res Int.* 2017;2017:9218486.

Abstract

Objective. Bradford Hill's viewpoints from 1965 on association or causation were used on glioma risk and use of mobile or cordless phones.

Methods. All nine viewpoints were evaluated based on epidemiology and laboratory studies.

Results. Strength: meta-analysis of case-control studies gave odds ratio (OR) = 1.90, 95% confidence interval (CI) = 1.31-2.76 with highest cumulative exposure. Consistency: the risk increased with latency, meta-analysis gave in the 10+ years' latency group OR = 1.62, 95% CI = 1.20-2.19. Specificity: increased risk for glioma was in the temporal lobe. Using meningioma cases as comparison group still increased the risk. Temporality: highest risk was in the 20+ years' latency group, OR = 2.01, 95% CI = 1.41-2.88, for wireless phones. Biological gradient:

cumulative use of wireless phones increased the risk. Plausibility: animal studies showed an increased incidence of glioma and malignant schwannoma in rats exposed to radiofrequency (RF) radiation. There is increased production of reactive oxygen species (ROS) from RF radiation. Coherence: there is a change in the natural history of glioma and increasing incidence. Experiment: antioxidants reduced ROS production from RF radiation. Analogy: there is an increased risk in subjects exposed to extremely low-frequency electromagnetic fields.

Conclusion. RF radiation should be regarded as a human carcinogen causing glioma.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5376454/>

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Wireless phone use and risk of adult glioma: Evidence from meta-analysis

Wang P, Hou C, Li Y, Zhou D. Wireless phone use and risk of adult glioma: Evidence from meta-analysis. *World Neurosurg.* 2018 Jul;115:e629-e636. doi: 10.1016/j.wneu.2018.04.122.

Objective Wireless phone use has been increasing rapidly and is associated with the risk of glioma. Many studies have been conducted on this association, but did not reach an agreement. The aim of this meta-analysis was to determine the possible association between wireless phone use and the risk of adult glioma.

Methods Eligible studies were identified by searching Pubmed and Embase till July 2017. The random- or fixed-effects model was used to combine the results depending on the heterogeneity of the analysis. Publication bias was evaluated using Begg's funnel plot and Egger's regression asymmetry test. Subgroup analysis was performed to evaluate the possible influence of these variables.

Results A total of 10 studies about the association of wireless phone use and the risk of glioma were included in this meta-analysis. The combined odd's ratio (OR) of adult glioma associated with ever use of wireless phone was 1.03 (95% CI=0.92–1.16) with high heterogeneity ($I^2=54.2\%$, $P=0.013$). In the subgroup analyses, no significant association was found among tumor location in the temporal lobe and adult glioma risk, with ORs of 1.26 (95% CI=0.87–1.84), 0.93 (95%CI=0.69–1.24), 1.61 (95%CI=0.78–3.33), respectively. Significant association was found in long-term users (≥ 10 years) with OR 1.33 (95%CI =1.05–1.67) and risk of glioma.

Conclusions Our analysis suggested that ever use of wireless phone was not significantly associated with the risk of adult glioma, but could increase the risk in long-term users.

<https://www.ncbi.nlm.nih.gov/pubmed/?term=29709736>

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Mobile phone use and glioma risk: A systematic review and meta-analysis

Yang M, Guo W, Yang C, Tang J, Huang Q, Feng S, Jiang A, Xu X, Jiang G. Mobile phone use and glioma risk: A systematic review and meta-analysis. PLoS One. 2017 May 4; 12(5):e0175136.

Abstract

OBJECTIVE: Many studies have previously investigated the potential association between mobile phone use and the risk of glioma. However, results from these individual studies are inconclusive and controversial. The objective of our study was to investigate the potential association between mobile phone use and subsequent glioma risk using meta-analysis.

METHODS: We performed a systematic search of the Science Citation Index Embase and PubMed databases for studies reporting relevant data on mobile phone use and glioma in 1980-2016. The data were extracted and measured in terms of the odds ratio (OR) and 95% confidence interval (CI) using the random effects model. Subgroup analyses were also carried out. This meta-analysis eventually included 11 studies comprising a total 6028 cases and 11488 controls.

RESULTS: There was a significant positive association between long-term mobile phone use (minimum, 10 years) and glioma (OR = 1.44, 95% CI = 1.08-1.91). And there was a significant positive association between long-term ipsilateral mobile phone use and the risk of glioma (OR = 1.46, 95% CI = 1.12-1.92). Long-term mobile phone use was associated with 2.22 times greater odds of low-grade glioma occurrence (OR = 2.22, 95% CI = 1.69-2.92). Mobile phone use of any duration was not associated with the odds of high-grade glioma (OR = 0.81, 95% CI = 0.72-0.92). Contralateral mobile phone use was not associated with glioma regardless of the duration of use. Similarly, this association was not observed when the analysis was limited to high-grade glioma.

CONCLUSIONS: Our results suggest that long-term mobile phone use may be associated with an increased risk of glioma. There was also an association between mobile phone use and low-grade glioma in the regular use or long-term use subgroups. However, current evidence is of poor quality and limited quantity. It is therefore necessary to conduct large sample, high quality research or better characterization of any potential association between long-term ipsilateral mobile phone use and glioma risk.

Open access paper: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0175136>

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Mobile phone use and risk of brain tumours: a systematic review of association between study quality, source of funding, and research outcomes

Prasad M, Kathuria P, Nair P, Kumar A, Prasad K. Mobile phone use and risk of brain tumours: a systematic review of association between study quality, source of funding, and research outcomes. Neurological Sciences. 38(5):797-810. 2017. doi: 10.1007/s10072-017-2850-8.

Abstract

Mobile phones emit electromagnetic radiations that are classified as possibly carcinogenic to humans. Evidence for increased risk for brain tumours accumulated in parallel by epidemiologic

investigations remains controversial. This paper aims to investigate whether methodological quality of studies and source of funding can explain the variation in results.

PubMed and Cochrane CENTRAL searches were conducted from 1966 to December 2016, which was supplemented with relevant articles identified in the references. Twenty-two case control studies were included for systematic review.

Meta-analysis of 14 case-control studies showed practically no increase in risk of brain tumour [OR 1.03 (95% CI 0.92-1.14)]. However, for mobile phone use of 10 years or longer (or 1,640 or more hours in lifetime), the overall result of the meta-analysis showed a significant 1.33 times increase in risk. The summary estimate of government funded as well as phone industry funded studies showed 1.07 times increase in odds which was not significant, while mixed funded studies did not show any increase in risk of brain tumour. Meta-regression analysis indicated that the association was significantly associated with methodological study quality ($p < 0.019$, 95% CI 0.009-0.09). Relationship between source of funding and log OR for each study was not statistically significant ($p < 0.32$, 95% CI 0.036-0.010).

We found evidence linking mobile phone use and risk of brain tumours especially in long-term users (10 or more years). Studies with higher quality showed a trend towards high risk of brain tumour, while lower quality showed a trend towards lower risk/protection.

<https://www.ncbi.nlm.nih.gov/pubmed/28213724>

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Mobile phone use and risk for intracranial tumors and salivary gland tumors - A meta-analysis

Bortkiewicz A, Gadzicka E, Szymczak W. Mobile phone use and risk for intracranial tumors and salivary gland tumors - A meta-analysis. *Int J Occup Med Environ Health*. 2017 Feb 21;30(1):27-43. doi: 10.13075/ijomeh.1896.00802.

Abstract

Results of epidemiological studies on the association between use of mobile phone and brain cancer are ambiguous, as well as the results of 5 meta-analysis studies published to date. Since the last meta-analysis (2009), new case-control studies have been published, which theoretically could affect the conclusions on this relationship. Therefore, we decided to perform a new meta-analysis. We conducted a systematic review of multiple electronic data bases for relevant publications. The inclusion criteria were: original papers, case-control studies, published till the end of March 2014, measures of association (point estimates as odds ratio and confidence interval of the effect measured), data on individual exposure. Twenty four studies (26 846 cases, 50 013 controls) were included into the meta-analysis. A significantly higher risk of an intracranial tumor (all types) was noted for the period of mobile phone use over 10 years (odds ratio (OR) = 1.324, 95% confidence interval (CI): 1.028-1.704), and for the ipsilateral location (OR = 1.249, 95% CI: 1.022-1.526). The results support the hypothesis that long-term use of mobile phone increases risk of intracranial tumors, especially in the case of ipsilateral exposure. Further studies are needed to confirm this relationship.

Excerpts

The results obtained in the random effects model indicated that there was a significant relationship between mobile phone use for longer than 10 years and the risk of intracranial tumors (OR = 1.46, 95% CI: 1.07–1.98).

Because OR is significantly greater than 1 (OR = 1.25, 95% CI: 1.04–1.52), we can conclude that there is a significant relationship between the time from the first regular use of mobile phone of 10 years or more and the risk of intracranial tumors.

Since OR is greater than 1 (OR = 1.29, 95% CI: 1.06–1.57), there is a significant relationship between ipsilateral use of mobile phone and the risk of intracranial tumor.

We found a significant relationship between:

- all intracranial tumors and all phone types; ipsilateral exposure;
- all intracranial tumors and all phone types, when the time of mobile phone use was not shorter than 10 years;
- all intracranial tumors and all phone types when the time from the first regular use of mobile phone was 10 years or more.

We are not able to compare our results with reference to different kinds of intracranial tumors (glioma, meningioma, acoustic neuroma) in relation to time of using mobile phones. A reliable analysis was not feasible because, in our opinion, the number of original works is too small.

Conclusions

Our results support the hypothesis that long-term (over 10 years) use of mobile phones increases the risk of intracranial tumors, especially in the case of ipsilateral exposure. The same conclusions are valid for the work by Davis et al. (2013) [45], who reviewed papers on the association between the use of wireless (mobile and cordless) phones and intracranial tumors. Those authors stress that the risk of tumors in people who have used the phone for periods longer than 10 years is significantly elevated. In people who had started using the phone on a regular basis before they were 20 years old, the risk of ipsilateral glioma was found to be fourfold higher. Hardell et al. (2013) [46] stress the significance of the “lifetime exposure dose.” For an exposure of ≥ 1640 h, the risk of ipsilateral acoustic neuroma is 2.55 (95% CI: 1.5–4.4).

These results are in concordance with the conclusion of the expert panel for the International Agency for Research on Cancer (IARC), that cell phones are possibly carcinogenic (Group 2B) [47]. More research is needed to confirm that electromagnetic fields emitted by mobile phones are carcinogenic to humans.

Open access paper: <http://ijomeh.eu/Mobile-phone-use-and-risk-for-intracranial-tumours-and-salivary-gland-tumours-A-meta-analysis,63713,0,2.html>

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Does cell phone use increase the chances of parotid gland tumor development? A systematic review and meta-analysis

de Siqueira EC, de Souza FT, Gomez RS, Gomes CC, de Souza RP. Does cell phone use

increase the chances of parotid gland tumor development? A systematic review and meta-analysis. J Oral Pathol Med. 2016 Dec 9. doi: 10.1111/jop.12531.

Abstract

BACKGROUND: Prior epidemiological studies had examined the association between cell phone use and the development of tumors in the parotid glands. However there is no consensus about the question of whether cell phone use is associated with increased risk of tumors in the parotid glands. We performed a meta-analysis to evaluate the existing literature about the mean question and to determine their statistical significance.

METHODS: Primary association studies. Papers that associated cell phone use and parotid gland tumors development were included, with no restrictions regarding publication date, language and place of publication. Systematic literature search using PubMed, Scielo and Embase followed by meta-analysis.

RESULTS AND CONCLUSION: Initial screening included 37 articles and three were included in meta-analysis. Using three independent samples including 5087 subjects from retrospective case-control studies, cell phone use seems to be associated with greater odds (1.28, 95%-confidence interval 1.09 - 1.51) to develop salivary gland tumor. Results should be read with caution due to the limited number of studies available and their retrospective design.

<https://www.ncbi.nlm.nih.gov/pubmed/27935126>

1.3. Oxidative stress and genotoxic effects - reviews

Effects of EMF exposure on the antioxidant defense system

Kivrak EG, Yurt KK, Kaplan AA, Alkan I, Altun G. Effects of electromagnetic fields exposure on the antioxidant defense system. J Microsc Ultrastruct. 2017 Oct-Dec;5(4):167-176.

Abstract

Technological devices have become essential components of daily life. However, their deleterious effects on the body, particularly on the nervous system, are well known. Electromagnetic fields (EMF) have various chemical effects, including causing deterioration in large molecules in cells and imbalance in ionic equilibrium. Despite being essential for life, oxygen molecules can lead to the generation of hazardous by-products, known as reactive oxygen species (ROS), during biological reactions. These reactive oxygen species can damage cellular components such as proteins, lipids and DNA. Antioxidant defense systems exist in order to keep free radical formation under control and to prevent their harmful effects on the biological system. Free radical formation can take place in various ways, including ultraviolet light, drugs, lipid oxidation, immunological reactions, radiation, stress, smoking, alcohol and biochemical redox reactions. Oxidative stress occurs if the antioxidant defense system is unable to prevent the harmful effects of free radicals. Several studies have reported that exposure to

EMF results in oxidative stress in many tissues of the body. Exposure to EMF is known to increase free radical concentrations and traceability and can affect the radical couple recombination. The purpose of this review was to highlight the impact of oxidative stress on antioxidant systems.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6025786/>

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Genotoxic and carcinogenic effects of non-ionizing electromagnetic fields

Kocaman A, Altun G, Kaplan AA, Deniz ÖG, Yurt KK, Kaplan S. Genotoxic and carcinogenic effects of non-ionizing electromagnetic fields. *Environ Res.* 2018 Feb 7;163:71-79. doi: 10.1016/j.envres.2018.01.034.

Abstract

New technologies in electronics and communications are continually emerging. An increasing use of these electronic devices such as mobile phone, computer, wireless fidelity connectors or cellular towers is raising questions concerning whether they have an adverse effect on the body. Exposure to electromagnetic fields (EMF) is frequently suggested to have adverse health effects on humans and other organisms. This idea has been reported in many studies. In contrast, the therapeutic effects of EMF on different organs have also been reported. Research findings are inconsistent. This has given rise to very profound discrepancies. The duration and frequency of mobile phone calls and the association observed with various health effects has raised serious concerns due to the frequency with which these devices are used and the way they are held close to the head. The present review assesses the results of in vitro, in vivo, experimental, and epidemiological studies. The purpose of the study is to assess data concerning the carcinogenic and genotoxic effects of non-ionizing EMF. The major genotoxic and carcinogenic effects of EMF, divided into subsections as low frequency effects and radiofrequency effects, were reviewed. The inconsistent results between similar studies and the same research groups have made it very difficult to make any comprehensive interpretation. However, evaluation of current studies suggests that EMF may represent a serious source of concern and may be hazardous to living organisms.

<https://www.ncbi.nlm.nih.gov/pubmed/29427953>

1.4. Reproductive harm - reviews

Proteomic impacts of electromagnetic fields on the male reproductive system

Sepehrimanesh, M. & Davis, D.L. Proteomic impacts of electromagnetic fields on the male reproductive system. *Comp Clin Pathol.* 26(2):309-313. 2016. doi:10.1007/s00580-016-2342-x . March 2017.

Abstract

The use of mobile phones and other wireless transmitting devices is increasing dramatically in developing and developed countries, as is the rate of infertility. A number of respected infertility

clinics in Australia, India, USA, and Iran are reporting that those who regularly use mobile phones tend to have reduced sperm quantity and quality. Some experimental studies have found that human sperm exposed to electromagnetic fields (EMF), either simulated or from mobile phones, developed biomarkers of impaired structure and function, as well as reduced quantity. These encompass pathological, endocrine, and proteomic changes. Proteins perform a vast array of functions within living organisms, and the proteome is the entire array of proteins—the ultimate biomolecules in the pathways of DNA transcription to translation. Proteomics is the art and science of studying all proteins in cells, using different techniques. This paper reviews proteomic experimental and clinical evidence that EMF acts as a male-mediated teratogen and contributor to infertility.

<http://link.springer.com/article/10.1007%2Fs00580-016-2342-x>

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Genomic effects of cell phone exposure on the reproductive system

Yahyazadeh A, Deniz OG, Kaplan AA, Altun G, Yurt KK, Davis D. The genomic effects of cell phone exposure on the reproductive system. *Environmental Research*. Available online 5 June 2018. <https://doi.org/10.1016/j.envres.2018.05.017>

Abstract

Humans are exposed to increasing levels of electromagnetic fields (EMF) at various frequencies as technology advances. In this context, improving understanding of the biological effects of EMF remains an important, high priority issue. Although a number of studies in this issue and elsewhere have focused on the mechanisms of the oxidative stress caused by EMF, the precise understanding of the processes involved remains to be elucidated. Due to unclear results among the studies, the issue of EMF exposure in the literature should be evaluated at the genomic level on the reproductive system. Based on this requirement, a detail review of recently published studies is necessary. The main objectives of this study are to show differences between negative and positive effect of EMF on the reproductive system of animal and human. Extensive review of literature has been made based on well known data bases like Web of Science, PubMed, MEDLINE, Google Scholar, Science Direct, Scopus. This paper reviews the current literature and is intended to contribute to a better understanding of the genotoxic effects of EMF emitted from mobile phones and wireless systems on the human reproductive system, especially on fertility. The current literature reveals that mobile phones can affect cellular functions via non-thermal effects. Although the cellular targets of global system for mobile communications (GSM)-modulated EMF are associated with the cell membrane, the subject is still controversial. Studies regarding the genotoxic effects of EMF have generally focused on DNA damage. Possible mechanisms are related to ROS formation due to oxidative stress. EMF increases ROS production by enhancing the activity of nicotinamide adenine dinucleotide (NADH) oxidase in the cell membrane. Further detailed studies are needed to elucidate DNA damage mechanisms and apoptotic pathways during oogenesis and spermatogenesis in germ cells exposed to EMF.

Conclusion

This paper reviews the current literature and is intended to contribute to a better understanding of the genotoxic effects of EMF emitted from mobile phones and wireless systems on the human reproductive system, especially on fertility. The current literature reveals that mobile phones can affect cellular functions via non-thermal effects (Diem et al., 2005; Hanci et al., 2013 ; Odaci et al., 2016a). Although the cellular targets of GSM-modulated EMF are associated with the cell membrane, the subject is still controversial (Eberhardt et al., 2008). Studies regarding the genotoxic effects of EMF have generally focused on DNA damage (Mortelmans and Rupa, 2004; Young, 2002; Zeiger, 2004; Panagopoulos, 2012 ; Turedi et al., 2016). Possible mechanisms are related to ROS formation due to oxidative stress (Moustafa et al., 2004; Hanukoglu et al., 2006). EMF increases ROS production by enhancing the activity of NADH oxidase in the cell membrane (Friedman et al., 2007b). In this context, EMF affected spermatozoa may have a high degree rate of infertilization. It seems that previous genomic studies do not show definitive evidence regarding EMF affected cells in the fertilization. Although we evaluated broadly the genomic effects of cell phone exposure on the reproductive system using both animal and human studies, one of the weaknesses of this work is insufficient review of human studies. This may come from limited number of EMF based human studies in the literature. Further detailed studies are needed to elucidate DNA damage mechanisms and apoptotic pathways during oogenesis and spermatogenesis in germ cells that are exposed to EMF.

<https://www.sciencedirect.com/science/article/pii/S0013935118302639>

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Effects of mobile phone exposure on metabolomics in the male and female reproductive systems

Altun G, Deniz OG, Yurt KK, Davis D, Kaplan S. Effects of mobile phone exposure on metabolomics in the male and female reproductive systems. *Environmental Research*. Available online 5 June 2018. <https://doi.org/10.1016/j.envres.2018.02.031>

Highlights

- Long-term exposure to EMF decreases sperm motility and fertilization.
- Effects of EMF emitted from mobile phones are related to protein synthesis.
- Oxidative stress based EMF exposure modulates nitric oxide level in the germ cells.
- Oxidative stress based EMF exposure inhibits antioxidant mechanisms in the germ cells.

Abstract

With current advances in technology, a number of epidemiological and experimental studies have reported a broad range of adverse effects of electromagnetic fields (EMF) on human health. Multiple cellular mechanisms have been proposed as direct causes or contributors to these biological effects. EMF-induced alterations in cellular levels can activate voltage-gated calcium channels and lead to the formation of free radicals, protein misfolding and DNA

damage. Because rapidly dividing germ cells go through meiosis and mitosis, they are more sensitive to EMF in contrast to other slower-growing cell types. In this review, possible mechanistic pathways of the effects of EMF exposure on fertilization, oogenesis and spermatogenesis are discussed. In addition, the present review also evaluates metabolomic effects of GSM-modulated EMFs on the male and female reproductive systems in recent human and animal studies. In this context, experimental and epidemiological studies which examine the impact of mobile phone radiation on the processes of oogenesis and spermatogenesis are examined in line with current approaches.

Conclusion

EMF emitted by mobile phones has a number of well-documented adverse metabolomic effects on the male and female reproductive systems and can lead to infertility by increasing ROS production and reducing GSH and other antioxidants. The primary target of the EMF emitted by mobile phones may be the cell membrane (Pall in press, this volume). This then results in accelerated activity of membrane NADH oxidase and, consequently, greater rates of ROS formation that cannot be easily conjugated or detoxified. Although many studies have reported morphological and functional deteriorations in testis and ovary following EMF exposures, as well both structural and functional deficits in reproductive health, the underlying mechanisms have not been fully elucidated. To assist in further clarification of these processes and mechanisms, Table 1 summarizes key studies on the metabolomic effects of EMF on reproductive systems. Future studies will benefit greatly from standardized exposure protocols and evaluations of key metabolomic indicators.

<https://www.sciencedirect.com/science/article/pii/S0013935118300999>

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The effects of radiofrequency electromagnetic radiation on sperm function

Houston BJ, Nixon B, King BV, De Iulius GN, Aitken RJ. The effects of radiofrequency electromagnetic radiation on sperm function. *Reproduction*. 2016 Dec;152(6):R263-R276. Epub 2016 Sep 6. DOI: 10.1530/REP-16-0126

Abstract

Mobile phone usage has become an integral part of our lives. However, the effects of the radiofrequency electromagnetic radiation (RF-EMR) emitted by these devices on biological systems and specifically the reproductive systems are currently under active debate. A fundamental hindrance to the current debate is that there is no clear mechanism of how such non-ionising radiation influences biological systems. Therefore, we explored the documented impacts of RF-EMR on the male reproductive system and considered any common observations that could provide insights on a potential mechanism. Among a total of 27 studies investigating the effects of RF-EMR on the male reproductive system, negative consequences of exposure were reported in 21. Within these 21 studies, 11 of the 15 that investigated sperm motility reported significant declines, 7 of 7 that measured the production of reactive oxygen species (ROS) documented elevated levels and 4 of 5 studies that probed for DNA damage highlighted increased damage due to RF-EMR exposure. Associated with this, RF-EMR treatment reduced the antioxidant levels in 6 of 6 studies that discussed this phenomenon, whereas consequences of RF-EMR were successfully ameliorated with the supplementation of antioxidants in all 3 studies that carried out these experiments. In light of this, we envisage a two-step mechanism

whereby RF-EMR is able to induce mitochondrial dysfunction leading to elevated ROS production. A continued focus on research, which aims to shed light on the biological effects of RF-EMR will allow us to test and assess this proposed mechanism in a variety of cell types.

<https://www.ncbi.nlm.nih.gov/pubmed/27601711>

1.5. Cardiovascular disease - review

Cardiovascular disease: Time to identify emerging environmental risk factors

Bandara P, Weller S. Cardiovascular disease: Time to identify emerging environmental risk factors. *Eur J Prev Cardio*. October 3, 2017. <https://doi.org/10.1177/2047487317734898>

No Abstract

Excerpts

In our latest review, 242 RF-EMR studies that investigated experimental endpoints related to oxidative stress (OS) were identified. A staggering 216 (89%) of them found significant effects related to OS, similar to a previous review. These are being further analysed following presentation at the recent Australasian Radiation Protection Society conference. Mostly in-vivo animal studies and in-vitro studies have demonstrated increased markers of endogenous OS and/or affected antioxidant levels in different tissue/cell types upon exposure to RF-EMR. Some studies have further demonstrated amelioration of RF-induced OS upon treatment with various antioxidants. Limited human studies at this stage complement these studies demonstrating OS and/or reduced antioxidant status upon acute radiofrequency exposure under experimental settings, in mobile phone users and residents near mobile phone base stations. Renowned physical scientists have recently presented experimental evidence and a theoretical explanation on how low-intensity RF-EMR can generate OS .

OS is known to be implicated in CVD and therefore RF-EMR, a new ubiquitous environmental exposure, may contribute to CVD by maintaining chronic OS, and thereby causing oxidative damage to cellular constituents and altering signal transduction pathways.

Although a few western countries have recently taken steps to reduce public exposure to RF-EMR, particularly of children, such as discouraging the use of wireless devices by children and banning/restricting WiFi in schools, there is largely inaction at this stage. Intriguingly, a professor in public health at the University of California recently went to court and accessed the cell phone safety 'fact sheet' (on health risks with instructions to reduce exposure) prepared by the Californian Department of Public Health. It is reported that this document, originally prepared in 2009 and revised 27 times up to 2014, was abandoned due to influences from vested interests. Meanwhile in France, a physician took legal action to access data from government testing of mobile phones revealing that most phones would not even pass the entirely thermally based (tissue heating) current exposure standards if held directly against the body, such as in a garment pocket.

It is clearly time to investigate the potential role of RF-EMR exposure from common wireless device use on CVD. Noting that existing research findings are influenced by the funding source, fresh directives are necessary for objective high quality research to expand current primary and secondary prevention strategies.

<http://journals.sagepub.com/doi/full/10.1177/2047487317734898>

1.6. Anticipated effects of 5G (5th generation cellular technology) - reviews

5G wireless telecommunications expansion: Public health and environmental implications

Russell CL. 5G wireless telecommunications expansion: Public health and environmental implications. *Environmental Research*. 165:484-495. August 2018.

Abstract

The popularity, widespread use and increasing dependency on wireless technologies has spawned a telecommunications industrial revolution with increasing public exposure to broader and higher frequencies of the electromagnetic spectrum to transmit data through a variety of devices and infrastructure. On the horizon, a new generation of even shorter high frequency 5G wavelengths is being proposed to power the Internet of Things (IoT). The IoT promises us convenient and easy lifestyles with a massive 5G interconnected telecommunications network, however, the expansion of broadband with shorter wavelength radiofrequency radiation highlights the concern that health and safety issues remain unknown. Controversy continues with regards to harm from current 2G, 3G and 4G wireless technologies. 5G technologies are far less studied for human or environmental effects.

It is argued that the addition of this added high frequency 5G radiation to an already complex mix of lower frequencies, will contribute to a negative public health outcome both from both physical and mental health perspectives.

Radiofrequency radiation (RF) is increasingly being recognized as a new form of environmental pollution. Like other common toxic exposures, the effects of radiofrequency electromagnetic radiation (RF EMR) will be problematic if not impossible to sort out epidemiologically as there no longer remains an unexposed control group. This is especially important considering these effects are likely magnified by synergistic toxic exposures and other common health risk behaviors. Effects can also be non-linear. Because this is the first generation to have cradle-to-grave lifespan exposure to this level of man-made microwave (RF EMR) radiofrequencies, it will be years or decades before the true health consequences are known. Precaution in the roll out of this new technology is strongly indicated.

This article will review relevant electromagnetic frequencies, exposure standards and current

scientific literature on the health implications of 2G, 3G, 4G exposure, including some of the available literature on 5G frequencies. The question of what constitutes a public health issue will be raised, as well as the need for a precautionary approach in advancing new wireless technologies.

<https://www.ncbi.nlm.nih.gov/pubmed/29655646>

Conclusion

Although 5G technology may have many unimagined uses and benefits, it is also increasingly clear that significant negative consequences to human health and ecosystems could occur if it is widely adopted. Current radiofrequency radiation wavelengths we are exposed to appear to act as a toxin to biological systems. A moratorium on the deployment of 5G is warranted, along with development of independent health and environmental advisory boards that include independent scientists who research biological effects and exposure levels of radiofrequency radiation. Sound regulatory policy regarding current and future telecommunications initiative will require more careful assessment of risks to human health, environmental health, public safety, privacy, security and social consequences. Public health regulations need to be updated to match appropriate independent science with the adoption of biologically based exposure standards prior to further deployment of 4G or 5G technology.

Considering the current science, lack of relevant exposure standards based on known biological effects and data gaps in research, we need to reduce our exposure to RF EMR wherever technically feasible. Laws or policies which restrict the full integrity of science and the scientific community with regards to health and environmental effects of wireless technologies or other toxic exposures should be changed to enable unbiased, objective and precautionary science to drive necessary public policies and regulation. Climate change, fracking, toxic emissions and microwave radiation from wireless devices all have something in common with smoking. There is much denial and confusion about health and environmental risks, along with industry insistence for absolute proof before regulatory action occurs (Frentzel-Beyme, 1994; Michaels 2008). There are many lessons we have not learned with the introduction of novel substances, which later became precarious environmental pollutants by not heeding warning signs from scientists (Gee, 2009). The threats of these common pollutants continue to weigh heavily on the health and wellbeing of our nation. We now accept them as the price of progress. If we do not take precautions but wait for unquestioned proof of harm will it be too late at that point for some or all of us?

<https://www.sciencedirect.com/science/article/pii/S0013935118300161>

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Towards 5G communication systems: Are there health implications?

Di Ciaula A. Towards 5G communication systems: Are there health implications? Int J Hyg Environ Health. 2018 Feb 2. pii: S1438-4639(17) 30814-3. doi: 10.1016/j.ijheh.2018.01.011.

Highlights

- RF-EMF exposure is rising and health effects of are still under investigation.
- Both oncologic and non-cancerous chronic effects have been suggested.
- 5G networks could have health effects and will use MMW, still scarcely explored.
- Adequate knowledge of RF-EMF biological effects is also needed in clinical practice.
- Underrating the problem could lead to a further rise in noncommunicable diseases.

Abstract

The spread of radiofrequency electromagnetic fields (RF-EMF) is rising and health effects are still under investigation. RF-EMF promote oxidative stress, a condition involved in cancer onset, in several acute and chronic diseases and in vascular homeostasis. Although some evidences are still controversial, the WHO IARC classified RF-EMF as "possible carcinogenic to humans", and more recent studies suggested reproductive, metabolic and neurologic effects of RF-EMF, which are also able to alter bacterial antibiotic resistance. In this evolving scenario, although the biological effects of 5G communication systems are very scarcely investigated, an international action plan for the development of 5G networks has started, with a forthcoming increment in devices and density of small cells, and with the future use of millimeter waves (MMW).

Preliminary observations showed that MMW increase skin temperature, alter gene expression, promote cellular proliferation and synthesis of proteins linked with oxidative stress, inflammatory and metabolic processes, could generate ocular damages, affect neuro-muscular dynamics. Further studies are needed to better and independently explore the health effects of RF-EMF in general and of MMW in particular. However, available findings seem sufficient to demonstrate the existence of biomedical effects, to invoke the precautionary principle, to define exposed subjects as potentially vulnerable and to revise existing limits. An adequate knowledge of pathophysiological mechanisms linking RF-EMF exposure to health risk should also be useful in the current clinical practice, in particular in consideration of evidences pointing to extrinsic factors as heavy contributors to cancer risk and to the progressive epidemiological growth of noncommunicable diseases.

<https://www.ncbi.nlm.nih.gov/pubmed/29402696>

1.7. Mechanisms

When theory and observation collide: Can non-ionizing radiation cause cancer?

Havas, M. When theory and observation collide: Can non-ionizing radiation cause cancer? Environ Pollut. 2017 Feb;221:501-505. doi: 10.1016/j.envpol.2016.10.018.

Highlights

- There is sufficient scientific evidence of cellular damage caused by non-ionizing radiation well below thermal guidelines.
- Applying the ionization model to non-ionizing radiation is inappropriate as mechanisms of biological interactions differ.
- Free radicals can and do cause cancer and non-ionizing radiation can and does increase free-radicals.

Abstract

This paper attempts to resolve the debate about whether non-ionizing radiation (NIR) can cause cancer—a debate that has been ongoing for decades. The rationale, put forward mostly by physicists and accepted by many health agencies, is that, “since NIR does not have enough energy to dislodge electrons, it is unable to cause cancer.” This argument is based on a flawed assumption and uses the model of ionizing radiation (IR) to explain NIR, which is inappropriate. Evidence of free-radical damage has been repeatedly documented among humans, animals, plants and microorganisms for both extremely low frequency (ELF) electromagnetic fields (EMF) and for radio frequency (RF) radiation, neither of which is ionizing. While IR directly damages DNA, NIR interferes with the oxidative repair mechanisms resulting in oxidative stress, damage to cellular components including DNA, and damage to cellular processes leading to cancer. Furthermore, free radical damage explains the increased cancer risks associated with mobile phone use, occupational exposure to NIR (ELF EMF and RFR), and residential exposure to power lines and RF transmitters including mobile phones, cell phone base stations, broadcast antennas, and radar installations.

<https://www.ncbi.nlm.nih.gov/pubmed/27903411>

Summary

This paper presents a highly probable mechanism that involves an increase in free-radicals, which—in turn—explains the increased risk of cancers documented in epidemiological studies that are associated with environmental exposure to RFR and ELF-EMFs at levels well below international guidelines.

<https://www.sciencedirect.com/science/article/pii/S0269749116309526>

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The role of electromagnetic fields in neurological disorders

Terzi M, Ozberk B, Deniz OG, Kaplan S. The role of electromagnetic fields in neurological disorders. *J Chem Neuroanat.* 2016 Sep;75(Pt B):77-84. doi: 10.1016/j.jchemneu.2016.04.003.

Abstract

In the modern world, people are exposed to electromagnetic fields (EMFs) as part of their daily lives; the important question is "What is the effect of EMFs on human health?" Most previous studies are epidemiological, and we still do not have concrete evidence of EMF pathophysiology. Several factors may lead to chemical, morphological, and electrical alterations in the nervous system in a direct or indirect way. It is reported that non-ionizing EMFs have effects on animals and cells. The changes they bring about in organic systems may cause oxidative stress, which is essential for the neurophysiological process; it is associated with increased oxidization in species, or a reduction in antioxidant defense systems. Severe oxidative stress can cause imbalances in reactive oxygen species, which may trigger neurodegeneration. This review aims to detail these changes. Special attention is paid to the current data regarding EMFs' effects on neurological disease and associated symptoms, such as headache, sleep disturbances, and fatigue.

<https://www.ncbi.nlm.nih.gov/pubmed/27083321>

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Electromagnetic Fields and Stem Cell Fate: When Physics Meets Biology

Tamrin SH, Majedi FS, Tondar M, Sanati-Nezhad A, Hasani-Sadrabadi MM. Electromagnetic Fields and Stem Cell Fate: When Physics Meets Biology. *Rev Physiol Biochem Pharmacol.* 2016;171:63-97.

Abstract

Controlling stem cell (SC) fate is an extremely important topic in the realm of SC research. A variety of different external cues mainly mechanical, chemical, or electrical stimulations individually or in combination have been incorporated to control SC fate. Here, we will deconstruct the probable relationship between the functioning of electromagnetic (EMF) and SC fate of a variety of different SCs. The electromagnetic (EM) nature of the cells is discussed with the emphasis on the effects of EMF on the determinant factors that directly and/or indirectly influence cell fate. Based on the EM effects on a variety of cellular processes, it is believed that EMFs can be engineered to provide a controlled signal with the highest impact on the SC fate decision. Considering the novelty and broad applications of applying EMFs to change SC fate, it is necessary to shed light on many unclear mechanisms underlying this phenomenon.

<https://www.ncbi.nlm.nih.gov/pubmed/27515674>

2.0. Human Studies

2.1. Cancer epidemiology

Canadian data from INTERPHONE study of mobile phone use and head tumor risk reported for the first time

Since the [13-nation Interphone study](#) was published in 2010, several papers have been published that reanalyze the data to correct for biases in the original paper. In most instances the glioma risk estimates increased among long term or heavy mobile phone users after adjustment for study biases.

The following paper published in the *American Journal of Epidemiology* applies statistical adjustments to the Interphone data from Canada. The authors found that the risk estimate for glioma among the highest quartile of cell phone users increased after adjustment. Risk estimates for other types of head tumors did not change.

Although Canada participated in this study, the U.S. did not. The original Canadian Interphone study data which had not been reported previously found a statistically significant doubling of risk for glioma among the highest quartile of cell phone users (over 558 lifetime hours). In contrast, the original 13-nation Interphone study found a 1.4-fold increase in glioma among the highest decile of use (1640 or more lifetime hours). After adjustment for selection and recall bias, the 2.0 odds ratio originally found in Canada increased to 2.2. Among the potential explanations the authors provided for this disparity between Canada and the 13-nation study (which included Canadian data): "real differences in risk related to different communication technologies between Canada and other INTERPHONE countries."

Momoli F, Siemiatycki J, McBride ML, Parent M^É, Richardson L, Bedard D, Platt R, Vrijheid M, Cardis E, Krewski D. Probabilistic multiple-bias modelling applied to the Canadian data from the INTERPHONE study of mobile phone use and risk of glioma, meningioma, acoustic neuroma, and parotid gland tumors. *Am J Epidemiol.* 2017 May 23. doi: 10.1093/aje/kwx157.

Abstract

We undertook a re-analysis of the Canadian data from the thirteen-country INTERPHONE case-control study (2001-2004), which evaluated the association between mobile phone use and risk of brain, acoustic neuroma, and parotid gland tumors. The main publication of the multinational INTERPHONE study concluded that "biases and errors prevent a causal interpretation". We applied a probabilistic multiple-bias model to address possible biases simultaneously, using validation data from billing records and non-participant questionnaires as information on recall error and selective participation. Our modelling sought to adjust for these sources of uncertainty and to facilitate interpretation. For glioma, the odds ratio comparing highest quartile of use (over 558 lifetime hours) to non-regular users was 2.0 (95% confidence interval: 1.2, 3.4). The odds ratio was 2.2 (95% confidence interval: 1.3, 4.1) when adjusted for selection and recall biases. There was little evidence of an increase in the risk of meningioma, acoustic neuroma, or parotid gland tumors in relation to mobile phone use. Adjustments for selection and recall biases did not materially affect interpretation in our Canadian results.

<https://www.ncbi.nlm.nih.gov/pubmed/28535174>

Excerpts

The OR of 2.0 for glioma in the highest cumulative exposure category (558+ hours of cumulative call time) in the Canadian study is higher than the value of 1.4 in the highest cumulative exposure category (1640+ hours) in the international study (4). This may simply reflect sampling variability, differential biases between study centers, matching strategies, or real differences in risk related to different communication technologies between Canada and other INTERPHONE countries (see appendix of (27)).

Unlike in the Canadian data, the INTERPHONE multinational study found marked decreased risk associated with most measures of phone use and an increased risk only in the highest decile of use. The study Group concluded that “biases and errors prevent a causal interpretation” (4, pg.1). To the extent that the bias model applied in the present re-analysis of the Canadian data is reasonable, conventional modelling of existing data likely resulted in slight underestimation of the magnitude of associations; however, interpretation of bias-adjusted results would not have materially changed from the original Canadian results.

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Intracranial Distribution of Gliomas in Relation to Mobile Phone Exposure: Analyses From the INTERPHONE Study

Grell, K., Frederiksen, K., Schutz, J., Cardis, E., Armstrong, B., Siemiatycki, J., Krewski, D. R., McBride, M. L., Johansen, C., Auvinen, A., Hours, M., Blettner, M., Sadetzki, S., Lagorio, S., Yamaguchi, N., Woodward, A., Tynes, T., Feychting, M., Fleming, S. J., Swerdlow, A. J., Andersen, P. K. The Intracranial Distribution of Gliomas in Relation to Exposure From Mobile Phones: Analyses From the INTERPHONE Study. *Am J Epidemiol.* 184(11):818-828. 2016..

Abstract

When investigating the association between brain tumors and use of mobile telephones, accurate data on tumor position are essential, due to the highly localized absorption of energy in the human brain from the radio-frequency fields emitted. We used a point process model to investigate this association using information that included tumor localization data from the INTERPHONE Study (Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, and the United Kingdom). Our main analysis included 792 regular mobile phone users diagnosed with a glioma between 2000 and 2004. Similar to earlier results, we found a statistically significant association between the intracranial distribution of gliomas and the self-reported location of the phone. When we accounted for the preferred side of the head not being exclusively used for all mobile phone calls, the results were similar. The association was independent of the cumulative call time and cumulative number of calls. However, our model used reported side of mobile phone use, which is potentially

influenced by recall bias. The point process method provides an alternative to previously used epidemiologic research designs when one is including localization in the investigation of brain tumors and mobile phone use.

Excerpts

... the INTERPHONE Study (6) ... is the largest investigation of mobile phone use and brain tumors to have been carried out to date. INTERPHONE observed no increased glioma risk in mobile phone users except for the decile with the highest reported cumulative call time (>1,640 hours), with uncertain interpretation (6).

... increased occurrence of tumors in the part of the brain closest to the phone would be expected if there were a causal association.

... our aim was to use the 3-dimensional point process model of Grell et al. (31) to analyze the INTERPHONE localization data for glioma and thereby further investigate the association between glioma and mobile phone use. Our use of a case-only approach removed possible differential bias between cases and controls ...

Overall, levels of use were low compared with today's levels due to the period of data collection, 2000–2004, when mobile phones were less common.

The 3-dimensional distribution of gliomas within the brain was skewed towards the self-reported preferred ear for mobile phone use.

Our results concur with the observation of a statistically significant excess of gliomas on the self-reported side of mobile phone use (28).

Taken together, our results suggest that ever using a mobile phone regularly is associated with glioma localization in the sense that more gliomas occurred closer to the ear on the side of the head where the mobile phone was reported to have been used the most. However, this trend was not related to amount of mobile phone use, making it less likely that the association observed is caused by a relationship between mobile phone use and cancer risk. We cannot draw firm conclusions about cause and effect, but our approach has several strengths in comparison with traditional epidemiologic approaches. Our results may have been affected by recall bias in the reported side of phone use. Nevertheless, it provides an alternative for future research related to mobile phone use.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5152665/>

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Investigation of bias related to differences between case and control interview dates in five INTERPHONE countries

Turner MC, Sadetzki S, Langer CE, Villegas R, Figuerola J, Armstrong BK, Chetrit A, Giles GG, Krewski D, Hours M, McBride ML, Parent M-E, Richardson L, Siemiatycki J, Woodward A, Cardis E. Investigation of bias related to differences between case and control interview dates in five INTERPHONE countries. *Annals of Epidemiology*. 26(12):827-832 e2, Dec 2016.

Abstract

Purpose Associations between cellular telephone use and glioma risk have been examined in several epidemiological studies including the 13-country INTERPHONE study. Although results showed no positive association between cellular telephone use and glioma risk overall, no increased risk for long term users, and no exposure-response relationship, there was an elevated risk for those in the highest decile of cumulative call time. However, results may be biased as data were collected during a period of rapidly increasing cellular telephone use, and as controls were usually interviewed later in time than cases.

Methods Further analyses were conducted in a subset of five INTERPHONE study countries (Australia, Canada, France, Israel, New Zealand) using a post-hoc matching strategy to optimize proximity of case to control interview dates and age.

Results Though results were generally similar to the original INTERPHONE study, there was some attenuation of the reduced odds ratios and stronger positive associations among long term users and those in the highest categories for cumulative call time and number of calls (8-9th and 10th decile).

Conclusions Proximity and symmetry in timing of case to control interviews should be optimized when exposure patterns are changing rapidly with time.

<https://www.ncbi.nlm.nih.gov/pubmed/28340909>

2.2. Brain tumor incidence trends

Mobile phones, cordless phones and rates of brain tumors in different age groups in the Swedish National Inpatient Register and the Swedish Cancer Register during 1998-2015

Hardell L, Carlberg M. Mobile phones, cordless phones and rates of brain tumors in different age groups in the Swedish National Inpatient Register and the Swedish Cancer Register during 1998-2015. PLoS One. 12(10): e0185461. Published Oct 4, 2017.

Abstract

We used the Swedish Inpatient Register (IPR) to analyze rates of brain tumors of unknown type (D43) during 1998–2015. Average Annual Percentage Change (AAPC) per 100,000 increased with +2.06%, 95% confidence interval (CI) +1.27, +2.86% in both genders combined. A joinpoint was found in 2007 with Annual Percentage Change (APC) 1998–2007 of +0.16%, 95% CI -0.94, +1.28%, and 2007–2015 of +4.24%, 95% CI +2.87, +5.63%. Highest AAPC was found in the age group 20–39 years. In the Swedish Cancer Register the age-standardized incidence rate per 100,000 increased for brain tumors, ICD-code 193.0, during 1998–2015 with AAPC in men +0.49%, 95% CI +0.05, +0.94%, and in women +0.33%, 95% CI -0.29, +0.45%. The cases with brain tumor of unknown type lack morphological examination. Brain tumor diagnosis was based on cytology/histopathology in 83% for men and in 87% for women in 1980. This frequency increased to 90% in men and 88% in women in 2015. During the same time period CT and MRI imaging techniques were introduced and morphology is not always necessary for diagnosis. If

all brain tumors based on clinical diagnosis with CT or MRI had been reported to the Cancer Register the frequency of diagnoses based on cytology/histology would have decreased in the register. The results indicate underreporting of brain tumor cases to the Cancer Register. The real incidence would be higher. Thus, incidence trends based on the Cancer Register should be used with caution. Use of wireless phones should be considered in relation to the change of incidence rates.

Open access paper: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0185461>

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Brain tumors: rise in Glioblastoma incidence in England 1995–2015 suggests adverse environmental or lifestyle factor

Philips A, Henshaw DL, Lamburn G, O'Carroll M. Brain tumours: rise in Glioblastoma Multiforme incidence in England 1995–2015 suggests an adverse environmental or lifestyle factor. *viron Public Health*. 2018 Jun 24;2018:7910754. doi: 10.1155/2018/7910754

Highlights

- A clear description of the changing pattern in incidence of brain tumour types
- The study used extensive data from an official and recognised quality source
- The study included histological and morphological information
- The study identified a significant and concerning incidence time trend
- Some evidence is provided to help guide future research into causal mechanisms

Abstract

Objective To investigate detailed trends in malignant brain tumour incidence over a recent time period.

Methods UK Office of National Statistics (ONS) data covering 81,135 ICD10 C71 brain tumours diagnosed in England (1995–2015) were used to calculate incidence rates (ASR) per 100k person–years, age–standardised to the European Standard Population (ESP–2013).

Results We report a sustained and highly statistically significant ASR rise in glioblastoma multiforme (GBM) across all ages. The ASR for GBM more than doubled from 2.4 to 5.0, with annual case numbers rising from 983 to 2531. Overall, this rise is mostly hidden in the overall data by a reduced incidence of lower grade tumours.

Conclusions The rise is of importance for clinical resources and brain tumour aetiology. The rise cannot be fully accounted for by promotion of lower–grade tumours, random chance or improvement in diagnostic techniques as it affects specific areas of the brain and only one type of brain tumour. Despite the large variation in case numbers by age, the percentage rise is similar across the age groups which suggests widespread environmental or lifestyle factors may be responsible.

Open access paper: <https://www.hindawi.com/journals/jeph/2018/7910754/>

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Philips A, Henshaw DL, Lamburn G, O'Carroll MJ. Letter to the Editor. Authors' Comment on "Brain Tumours: Rise in Glioblastoma Multiforme Incidence in England 1995–2015 Suggests an Adverse Environmental or Lifestyle Factor." *J Environ Public Health*. 2018 Jun 25;2018:2170208. doi: 10.1155/2018/2170208. <https://doi.org/10.1155/2018/2170208>.

At the request of the Editor, we here provide further background to our article [1].

Over the past 20 years, the authors have been involved in organising international conferences on causes of cancer and finding precautionary actions that may help to reduce the ongoing overall rise in the cancer burden [2, 3]. As part of this, we follow trends in cancer incidence across all ages. We were hearing from clinicians that they were seeing an increase in aggressive brain tumours, especially glioblastoma multiforme (GBM), but cancer registries were generally reporting no significant overall increased incidence in brain tumours.

By 2008, we were seeing a statistically significant increased incidence in frontal and temporal lobe tumours and a decrease in tumour incidence at some other brain sites listed in UK Office for National Statistics (ONS) MB1 cancer data. In November 2011, three of the current authors discussed this rise during a two-day EC conference in Brussels. We were told by two leading European epidemiologists that if we could not see a clear trend in the overall data, there was no point in looking at underlying, more detailed data.

The rising incidence in frontal and temporal lobes continued to appear in the public MB1 data and we decided to formally test our suspicion that something important was changing. We applied for, and obtained, more detailed information from the ONS which included ICD-O-10 coding. As part of our ongoing monitoring, we have twice had these data updated. This resulted in our current article [1], where we report a clear increasing trend in GBM incidence over time. In the article, we also briefly discuss a number of different possible causal factors that have been reported in the scientific literature.

We acknowledge that published data from the US Central Brain Tumor Registry (CBTRUS) and the Surveillance, Epidemiology, and End Results (SEER) organisations do not report a similar rise in GBM. One factor will be that, according to CBTRUS, GBM incidence rate in black people is approximately half that for white people and has a different age-related profile [4]. The US has a higher percentage of black people compared with England and this will have some effect on the whole-population brain tumour data profile.

However, we have come to an initial conclusion that the main reason is due to (a) the US2000 Standard Population that they use to adjust their data and (b) the fact that they use age-standardised data even for age-grouped data that would usually be age-specific. Age-standardised data are used for comparing overall rates between countries and for following overall data trends within a country.

All the data in the CBTRUS reports (see Figure 13 in each reference [5, 6]) are stated as being adjusted to the US2000 Standard Population [7]. This does not reasonably represent the age spectrum of the current US population. This is shown in Figure 1.

Figure 1: US2000 Standard Population, the 2016 US actual population, and ESP2013.

The current US population is very different from the US2000 Standard Population. The effect of applying US2000 is to reduce, by about 30%, the overall contribution from cases in people aged 50 to 70 years. This is the age range of the majority of the cases in the ONS data which show the rising GBM incidence trend. Using US2000 gives added weight to the “healthy worker” age range (30 to 44), where relatively few GBM cases occur. It is important that the age standardisation profile is a reasonable fit to the current population age profile. We note that SEER updated the US Standard Population every ten years from 1940 to 2000 but have not done so since 2000 [6].

We offer, for discussion, Figure 2, where we have back-adjusted the US age-group data from US2000 to the actual US population data for 2008 and 2012 [8], along with English ONS data for two five-year periods from our article. The readjusted US data now show an increase in GBM similar to our findings. US data of unadjusted, age-specific GBM incidence rates for all 5-year age groups for every year from 2005 and 2015 are required to check our approximate correction.

Figure 2: Comparison of ONS and US data trends following adjustment to age-specific rate.

We would like to add to the discussion of potential risk factors in our article.

There is a growing body of evidence that exposure to air pollution, notably arising from the carcinogenic components of vehicle exhausts, such as PAHs, 1,3-butadiene, and diesel particulate matter generally, may be associated with increased risk of brain tumours in both children and adults. Studies in children, young adults, and canines indicate that inhaled ultrafine air pollution particles, ~100 nm, pass through the lung to reach and both damage and cross the blood-brain barrier (Calderón-Garcidueñas et al. (2008) [9], (2003) [10]).

Braüner et al. (2013) [11] reported an association between calculated domestic radon exposure and brain tumour incidence in a Danish cohort, with doubling of risk with each 100 Bq. increment in average residential radon levels. Indoor radon levels have increased in recent decades with the progressive introduction of double-glazed windows and general house sealing, resulting in lower rates of air changes with outside air.

Ostrom et al. [12] considered mobile phone use and judged that the current evidence “was inconclusive” but recommended continued monitoring of this issue. De Vocht (2016) [13] concluded that “A causal factor, of which mobile phone use (and possibly other wireless equipment) is in agreement with the hypothesized temporal association, is related to an increased risk of developing malignant neoplasms in the temporal lobe.” He later published an important correction to the article, showing a large rise in GBM tumour incidence with time [14]. The article reports that the GBM rise was not associated with his mobile phone use impact modelling, but we note that the model was only for primary initiation and not promotion of lower-grade tumours.

Our article does not focus on any particular risk factor to explain the rising incidence of aggressive GBM tumours, which are usually quickly fatal. We recommend that our detailed

analyses be repeated for cancer registry data in other countries. If our results are confirmed, then high priority should be given to identifying the factors involved in the rise.

<https://www.hindawi.com/journals/jep/2018/2170208/>

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Inferring the 1985–2014 impact of mobile phone use on selected brain cancer subtypes

Frank de Vocht. Inferring the 1985–2014 impact of mobile phone use on selected brain cancer subtypes using Bayesian structural time series and synthetic controls. *Environ Int.* 2016 Dec;97:100-107. doi: 10.1016/j.envint.2016.10.019.

Highlights

- English brain cancer subtypes incidences were compared to synthetic control trends.
- No evidence of increases in GBM, glioma and parietal lobe neoplasms not predicted.
- Malignant neoplasms of the temporal lobe however, have increased faster than expected.
- This corresponded to additional 35% increase, or 188 (95%CI 48–324) cases annually.
- Tumour location and temporal associations correspond with mobile phone use as risk factor.

Abstract

Background Mobile phone use has been increasing rapidly in the past decades and, in parallel, so has the annual incidence of certain types of brain cancers. However, it remains unclear whether this correlation is coincidental or whether use of mobile phones may cause the development, promotion or progression of specific cancers. The 1985–2014 incidence of selected brain cancer subtypes in England were analyzed and compared to counterfactual ‘synthetic control’ timeseries.

Methods Annual 1985–2014 incidence of malignant glioma, glioblastoma multiforme, and malignant neoplasms of the temporal and parietal lobes in England were modelled based on population-level covariates using Bayesian structural time series models assuming 5, 10 and 15 year minimal latency periods. Post-latency counterfactual ‘synthetic England’ timeseries were nowcast based on covariate trends. The impact of mobile phone use was inferred from differences between measured and modelled time series.

Results There is no evidence of an increase in malignant glioma, glioblastoma multiforme, or malignant neoplasms of the parietal lobe not predicted in the ‘synthetic England’ time series. Malignant neoplasms of the temporal lobe however, have increased faster than expected. A latency period of 10 years reflected the earliest latency period when this was measurable and related to mobile phone penetration rates, and indicated an additional increase of 35% (95% Credible Interval 9%:59%) during 2005–2014; corresponding to an additional 188 (95%CI 48–324) cases annually.

Conclusions A causal factor, of which mobile phone use (and possibly other wireless equipment) is in agreement with the hypothesized temporal association, is related to an increased risk of developing malignant neoplasms in the temporal lobe.

Excerpts

The annual incidence of malignant neoplasms of the temporal lobe however, has been increasing faster than expected, with a period of 10 years post-1995 reflecting the earliest latency period when this additional increase was measurable. Post-2005 an additional increase of 35% (95%CI 9%:59%) was evident compared to the counterfactual time series in the 'synthetic England'; corresponding to an average of an additional 188 (95%CI 48–324) cases of malignant neoplasms of the temporal lobe annually. Addition of mobile phone penetration in the models showed a reduction of 15% in the effect size for 5-year latency (Table 2), indicating observed increased incidence can, at least in part, be attributed to mobile phone use (Note that unfortunately longer latencies cannot be explored in these time series).

These analyses indicate excess brain cancer risk is observed in the lobes where most of the electromagnetic energy is absorbed (depending on side of the head where the phone is held when calling) (Cardis et al., 2008), which has been observed previously (Barchana et al., 2012 and Khurana et al., 2009). As such, it does not specifically exclude a specific association with gliomas (if these occur in the temporal lobe), which was reported in Interphone (Interphone Study Group, 2010), and of which about one in three occur in the temporal lobe (Larjavaara et al., 2007). A stronger causal argument could have been made if these analyses could have been stratified by laterality, with ipsilateral RF exposure having been linked to increased cerebral blood flow (Huber et al., 2005) and glucose metabolism (Volkow et al., 2011), as well as to increased risk of glioma in the temporal lobe (Barchana et al., 2012 and Hardell and Carlberg, 2015), although not in all studies (Hartikka et al., 2009 and Larjavaara et al., 2011), but this was not possible.

In summary, these analyses indicate that a causal factor, of which mobile phone use (and possibly other wireless equipment) is in agreement with the hypothesized spatial and temporal associations, is related to an increased risk of developing a malignant neoplasm in the temporal lobe. More specifically, if the calculated population impact is interpreted as a causal effect and is completely contributed to mobile phone use, then the population impact is an additional 188 cases annually in England; corresponding to about 1700 cases (range 436 to 2918) in the period 2005–2014 that would not have occurred otherwise. For reference, this corresponds to 0.02%–0.12% of new cancers during this period. If the relative effect is interpreted as a population relative risk, then a very moderate 1.35 (95%CI 1.09:1.59) is observed after a minimum 10-year latency.

[https://linkinghub.elsevier.com/retrieve/pii/S0160-4120\(16\)30386-5](https://linkinghub.elsevier.com/retrieve/pii/S0160-4120(16)30386-5)

2.3. Reproductive harm

Maternal cell phone use during pregnancy and child behavioral problems in five birth cohorts

Birks L, Guxens M, Papadopoulou E, Alexander J, Ballester F, Estarlich M, Gallastegi M, Ha M, Haugen M, Huss A, Kheifets L et al. Maternal cell phone use during pregnancy and child behavioral problems in five birth cohorts. *Environment International*. 104:122-131. July, 2017. <http://doi.org/10.1016/j.envint.2017.03.024>

"This is the largest study to date to evaluate these associations and to show mostly consistent results across cohorts with retrospectively and prospectively assessed maternal cell phone use."

Highlights

- Largest study to date to use prenatal cell phone use data collected prospectively.
- High prenatal cell phone use linked to hyperactivity/inattention problems in child.
- No prenatal cell phone use linked to low risk for any behavioral problems in child.
- Analysis adjusted for many confounders, but associations cannot be judged causal.
- Future research should adjust for parenting style, maternal hyperactivity, and more.

Introduction Previous studies have reported associations between prenatal cell phone use and child behavioral problems, but findings have been inconsistent and based on retrospective assessment of cell phone use. This study aimed to assess this association in a multi-national analysis, using data from three cohorts with prospective data on prenatal cell phone use, together with previously published data from two cohorts with retrospectively collected cell phone use data.

Methods We used individual participant data from 83,884 mother-child pairs in the five cohorts from Denmark (1996–2002), Korea (2006–2011), the Netherlands (2003–2004), Norway (2004–2008), and Spain (2003–2008). We categorized cell phone use into none, low, medium, and high, based on frequency of calls during pregnancy reported by the mothers. Child behavioral problems (reported by mothers using the Strengths and Difficulties Questionnaire or Child Behavior Checklist) were classified in the borderline/clinical and clinical ranges using validated cut-offs in children aged 5–7 years. Cohort specific risk estimates were meta-analyzed.

Results Overall, 38.8% of mothers, mostly from the Danish cohort, reported no cell phone use during pregnancy and these mothers were less likely to have a child with overall behavioral, hyperactivity/inattention or emotional problems. Evidence for a trend of increasing risk of child behavioral problems through the maternal cell phone use categories was observed for hyperactivity/inattention problems (OR for problems in the clinical range: 1.11, 95% CI 1.01, 1.22; 1.28, 95% CI 1.12, 1.48, among children of medium and high users, respectively). This association was fairly consistent across cohorts and between cohorts with retrospectively and prospectively collected cell phone use data.

Conclusions Maternal cell phone use during pregnancy may be associated with an increased risk for behavioral problems, particularly hyperactivity/inattention problems, in the offspring. The interpretation of these results is unclear as uncontrolled confounding may influence both maternal cell phone use and child behavioral problems.

<https://www.ncbi.nlm.nih.gov/pubmed/28392066>

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Neurodevelopment for first 3 years following prenatal mobile phone use, RF radiation & lead exposure

Choi K-H, Ha M, Ha E-H, Park H, Kim Y, Hong Y-C, Lee A-K, Kwon JH, Choi H-D, Kim N, Kim S, Park C. Neurodevelopment for the first three years following prenatal mobile phone use, radio frequency radiation and lead exposure. *Environmental Research*, 156:810-817, July 2017.

Highlights

- RFR exposure was measured by mobile phone use questionnaire and 24-h personal exposure meter among pregnant women.
- Child neurodevelopment was assessed by trained examiners at 6, 12, 24, and 36 months of age.
- Associations were not observed between prenatal exposure to RFR and child neurodevelopment during the first three years.
- A potential combined effect of prenatal exposure to lead and mobile phone use was suggested.

Abstract

Background Studies examining prenatal exposure to mobile phone use and its effect on child neurodevelopment show different results, according to child's developmental stages.

Objectives To examine neurodevelopment in children up to 36 months of age, following prenatal mobile phone use and radiofrequency radiation (RFR) exposure, in relation to prenatal lead exposure.

Methods We analyzed 1198 mother-child pairs from a prospective cohort study (the Mothers and Children's Environmental Health Study). Questionnaires were provided to pregnant women at ≤ 20 weeks of gestation to assess mobile phone call frequency and duration. A personal exposure meter (PEM) was used to measure RFR exposure for 24 h in 210 pregnant women. Maternal blood lead level (BLL) was measured during pregnancy. Child neurodevelopment was assessed using the Korean version of the Bayley Scales of Infant Development-Revised at 6, 12, 24, and 36 months of age. Logistic regression analysis applied to groups classified by trajectory analysis showing neurodevelopmental patterns over time.

Results The psychomotor development index (PDI) and the mental development index (MDI) at 6, 12, 24, and 36 months of age were not significantly associated with maternal mobile phone use during pregnancy. However, among children exposed to high maternal BLL in utero, there was a significantly increased risk of having a low PDI up to 36 months of age, in relation to an increasing average calling time (p -trend=0.008). There was also a risk of having decreasing MDI up to 36 months of age, in relation to an increasing average calling time or frequency during pregnancy (p -trend=0.05 and 0.007 for time and frequency, respectively). There was no significant association between child neurodevelopment and prenatal RFR exposure measured by PEM in all subjects or in groups stratified by maternal BLL during pregnancy.

Conclusions We found no association between prenatal exposure to RFR and child neurodevelopment during the first three years of life; however, a potential combined effect of prenatal exposure to lead and mobile phone use was suggested.

<https://www.ncbi.nlm.nih.gov/pubmed/28511138>

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Mobile phone use during pregnancy with birth weight: Kumamoto of Japan Environment and Children's Study

Lu X, Oda M, Ohba T, Mitsubuchi H, Masuda S, Kato T. Association of excessive mobile

phone use during pregnancy with birth weight: an adjunct study in Kumamoto of Japan Environment and Children's Study. *Environ Health Prev Med.* 2017 Jun 8;22(1):52. doi: 10.1186/s12199-017-0656-1.

Abstract

BACKGROUND: Low birth weight has been shown to be closely associated with neonatal mortality and morbidity, inhibited growth, poor cognitive development, and chronic diseases later in life. Some studies have also shown that excessive mobile phone use in the postnatal period may lead to behavioral complications in the children during their growing years; however, the relationship between mobile phone use during pregnancy and neonatal birth weight is not clear. The aim of the present study was to determine the associations of excessive mobile phone use with neonatal birth weight and infant health status.

METHODS: A sample of 461 mother and child pairs participated in a survey on maternal characteristics, infant characteristics, and maternal mobile phone usage information during pregnancy.

RESULTS: Our results showed that pregnant women tend to excessively use mobile phones in Japan. The mean infant birth weight was lower in the excessive use group than in the ordinary use group, and the frequency of infant emergency transport was significantly higher in the excessive use group than in the ordinary use group.

CONCLUSIONS: Excessive mobile phone use during pregnancy may be a risk factor for lower birth weight and a high rate of infant emergency transport.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5664573/>

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Combined effects of varicocele and cell phones on semen and hormonal parameters

Schauer I, Mohamad Al-Ali B. Combined effects of varicocele and cell phones on semen and hormonal parameters. *Wien Klin Wochenschr.* 2018 May;130(9-10):335-340. doi: 10.1007/s00508-017-1277-9.

Abstract

BACKGROUND: The objective of this study was to evaluate if there is a combined effect of varicocele and cell phone storage in trousers pockets on semen and hormonal parameters.

METHODS: A retrospective analysis of 468 men attending an infertility clinic from 1993-2007 was performed. Varicoceles were determined by clinical examination and patients were questioned on cell phone usage and storage fashion. Semen samples were analyzed according to the World Health Organization (WHO) guidelines of 1999. Serum testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH) were assessed.

RESULTS: There was a significant effect of cell phone storage in trousers pockets and varicocele in multivariate analysis (both $p < 0.001$). Varicocele showed an effect on sperm concentration ($p = 0.003$), LH ($p = 0.014$) and testosterone ($p = 0.003$). Compared to grade 1, grade 2 varicoceles showed a difference in sperm concentration ($p = 0.004$). Regarding testosterone differences were shown for grade 3 versus grade 1 ($p = 0.002$) and grade 3 compared to grade 2 ($p = 0.003$). Cell phone storage in trousers pockets showed an influence on the percentage of normal sperm morphology and LH (both $p < 0.001$). Varicocele and cell phone storage in trousers pockets did not show a combined effect ($p = 0.76$).

CONCLUSIONS: This analysis showed an inverse relation between sperm concentration and degree of varicocele, with lower concentrations in higher grade varicoceles. Testosterone was significantly higher in higher grade varicoceles, which could reflect a compensatory mechanism to the impaired testicular function. Cell phone storage in trousers pockets showed an effect on LH and sperm morphology. A combined effect of varicocele and cell phone storage in trousers pockets was not detected.

<https://www.ncbi.nlm.nih.gov/pubmed/29030685>

2.4. Cognitive and memory effects

Cohort study of adolescents' memory performance & brain dose of microwave radiation from wireless EMF

Foerster M., Thielens A., Joseph W., Eeftens M., Rösli M. A prospective cohort study of adolescents' memory performance and individual brain dose of microwave radiation from wireless communication. *Environmental Health Perspectives*. 126(7). 2018.
DOI:10.1289/EHP2427

Abstract

BACKGROUND: The potential impact of microwave radiofrequency electromagnetic fields (RF-EMF) emitted by wireless communication devices on neurocognitive functions of adolescents is controversial. In a previous analysis, we found changes in figural memory scores associated with a higher cumulative RF-EMF brain dose in adolescents.

OBJECTIVE: We aimed to follow-up our previous results using a new study population, dose estimation, and approach to controlling for confounding from media usage itself.

METHODS: RF-EMF brain dose for each participant was modeled. Multivariable linear regression models were fitted on verbal and figural memory score changes over 1 y and on estimated cumulative brain dose and RF-EMF related and unrelated media usage ($n=669-676$). Because of the hemispheric lateralization of memory, we conducted a laterality analysis for phone call ear preference. To control for the confounding of media use behaviors, a stratified analysis for different media usage groups was also conducted.

RESULTS: We found decreased figural memory scores in association with an interquartile

range (IQR) increase in estimated cumulative RF-EMF brain dose scores: -0.22 (95% CI: $-0.47, 0.03$; IQR: 953 mJ=kg per day) in the whole sample, -0.39 (95% CI: $-0.67, -0.10$; IQR: 953 mJ=kg per day) in right-side users ($n=532$), and -0.26 (95% CI: $-0.42, -0.10$; IQR: 341 mJ=kg per day) when recorded network operator data were used for RF-EMF dose estimation ($n=274$). Media usage unrelated to RF-EMF did not show significant associations or consistent patterns, with the exception of consistent (nonsignificant) positive associations between data traffic duration and verbal memory.

CONCLUSIONS: Our findings for a cohort of Swiss adolescents require confirmation in other populations but suggest a potential adverse effect of RF-EMF brain dose on cognitive functions that involve brain regions mostly exposed during mobile phone use.

Conclusion

We found preliminary evidence suggesting that RF-EMF may affect brain functions such as figural memory in regions that are most exposed during mobile phone use. Our findings do not provide conclusive evidence of causal effects and should be interpreted with caution until confirmed in other populations. Associations with media use parameters with low RF-EMF exposures did not provide clear or consistent support of effects of media use unrelated to RF-EMF (with the possible exception of consistent positive associations between verbal memory and data traffic duration). It is not yet clear which brain processes could be potentially affected and what biophysical mechanism may play a role. Potential long-term risk can be minimized by avoiding high brain-exposure situations as occurs when using a mobile phone with maximum power close to the ear because of, for example, bad network quality.

Open access paper: <https://ehp.niehs.nih.gov/EHP2427/>

2.5. Other effects

Heart rate variability affected by RF EMF in adolescent students

Misek J, Belyaev I, Jakusova V, Tonhajzerova I, Barabas J, Jakus J. Heart rate variability affected by radiofrequency electromagnetic field in adolescent students. *Bioelectromagnetics*. 2018 May;39(4):277-288. doi: 10.1002/bem.22115.

Abstract

This study examines the possible effect of radiofrequency (RF) electromagnetic fields (EMF) on the autonomic nervous system (ANS). The effect of RF EMF on ANS activity was studied by measuring heart rate variability (HRV) during ortho-clinostatic test (i.e., transition from lying to standing and back) in 46 healthy grammar school students. A 1788 MHz pulsed wave with intensity of 54 ± 1.6 V/m was applied intermittently for 18 min in each trial. Maximum specific absorption rate (SAR₁₀) value was determined to 0.405 W/kg. We also measured the respiration rate and estimated a subjective perception of EMF exposure. RF exposure

decreased heart rate of subjects in a lying position, while no such change was seen in standing students. After exposure while lying, a rise in high frequency band of HRV and root Mean Square of the Successive Differences was observed, which indicated an increase in parasympathetic nerve activity. Tympanic temperature and skin temperature were measured showing no heating under RF exposure. No RF effect on respiration rate was observed. None of the tested subjects were able to distinguish real exposure from sham exposure when queried at the end of the trial. In conclusion, short-term RF EMF exposure of students in a lying position during the ortho-clinostatic test affected ANS with significant increase in parasympathetic nerve activity compared to sham exposed group.

<https://www.ncbi.nlm.nih.gov/pubmed/29469164>

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Mobile phone EMF induced DNA damage in human ear canal hair follicle cells

Akdag M, Dasdag S, Canturk F, Akdag MZ. Exposure to non-ionizing electromagnetic fields emitted from mobile phones induced DNA damage in human ear canal hair follicle cells. *Electromagn Biol Med*. 2018 Apr 18:1-10. doi: 10.1080/15368378.2018.1463246.

Abstract

The aim of this study was to investigate effect of radiofrequency radiation (RFR) emitted from mobile phones on DNA damage in follicle cells of hair in the ear canal. The study was carried out on 56 men (age range: 30-60 years old) in four treatment groups with n = 14 in each group. The groups were defined as follows: people who did not use a mobile phone (Control), people use mobile phones for 0-30 min/day (second group), people use mobile phones for 30-60 min/day (third group) and people use mobile phones for more than 60 min/day (fourth group). Ear canal hair follicle cells taken from the subjects were analyzed by the Comet Assay to determine DNA damages. The Comet Assay parameters measured were head length, tail length, comet length, percentage of head DNA, tail DNA percentage, tail moment, and Olive tail moment. Results of the study showed that DNA damage indicators were higher in the RFR exposure groups than in the control subjects. In addition, DNA damage increased with the daily duration of exposure. In conclusion, RFR emitted from mobile phones has a potential to produce DNA damage in follicle cells of hair in the ear canal. Therefore, mobile phone users have to pay more attention when using wireless phones.

<https://www.ncbi.nlm.nih.gov/pubmed/29667447>

Excerpts

Participants using smart phones with similar SAR values, were used. The head peak SAR values of the smart phones used by the participants, ranged between 0.45–0.97 W/kg.

Comet Assay was performed by researchers who were unaware of which group the hair samples were from.

In conclusion, the findings of the present study indicated that exposure to radiation from mobile phones can lead to DNA single-strand breaks, therefore, to DNA damage. The results of this study indicated a positive correlation between duration of exposure and DNA damage. We consider that the result of this study might be important in terms of the balance involved in DNA damage and repair mechanisms.

2.6. Children's exposure to cell phone radiation

Wireless radiation absorption in child vs adult brain & eye from cell phone conversation or virtual reality

Fernandez C, de Salles AA, Sears ME, Morris RD, Davis DL. Absorption of wireless radiation in the child versus adult brain and eye from cell phone conversation or virtual reality. *Environ Res.* 2018 May 22. pii: S0013-9351(18)30256-1. doi: 10.1016/j.envres.2018.05.013.

Highlights

- More cell phone radiation is absorbed by children's inner brain tissues than adults'.
- Children's radiofrequency radiation exposure should be reduced.
- Further research to evaluate the risks to the eye from use of VR is urgently needed.
- It is biologically relevant and feasible to reduce the standards' averaging volume.
- Current methods to determine wireless device compliance should be revised.

Abstract

Children's brains are more susceptible to hazardous exposures, and are thought to absorb higher doses of radiation from cell phones in some regions of the brain. Globally the numbers and applications of wireless devices are increasing rapidly, but since 1997 safety testing has relied on a large, homogenous, adult male head phantom to simulate exposures; the "Standard Anthropomorphic Mannequin" (SAM) is used to estimate only whether tissue temperature will be increased by more than 1 Celsius degree in the periphery. The present work employs anatomically based modeling currently used to set standards for surgical and medical devices, that incorporates heterogeneous characteristics of age and anatomy. Modeling of a cell phone held to the ear, or of virtual reality devices in front of the eyes, reveals that young eyes and brains absorb substantially higher local radiation doses than adults'. Age-specific simulations indicate the need to apply refined methods for regulatory compliance testing; and for public education regarding manufacturers' advice to keep phones off the body, and prudent use to limit exposures, particularly to protect the young.

<https://www.ncbi.nlm.nih.gov/pubmed/29884550>

Excerpts

In summary, compared with adult models, children experience two- to three-fold higher RF doses to: 1) localized areas of the brain when a cell phone is positioned next to the ear; and 2) the eyes and frontal lobe when a cell phone is used to view virtual reality. These findings raise serious questions about the current approach to certify cell phones; particularly the use of the SAM.

Our modeling demonstrates clearly that localized psSAR varies significantly for critical components of the brain. Younger models absorb proportionally more radiation in the eyes and brain – grey matter, cerebellum and hippocampus—and the local dose rate varies inversely with age. This reflects the fact that the head is not homogeneous. Indeed, localized heating up to 5 Centigrade degrees has been detected as a result of mobile phone radiation studied *ex vivo* in cow brain using Nuclear Magnetic Resonance thermometry (Gultekin and Moeller, 2013).

Our findings support reexamination of methods to determine regulatory compliance for wireless devices, and highlight the importance of precautionary advice such as that of American Academy of Pediatrics (2016). The Academy recommends that younger children should not use cell phones, and that prudent measures should be taken to eliminate exposure (e.g. using devices for amusement or education only when all wireless features are turned off – in “airplane mode”) or to minimize exposure (e.g. texting or using speakerphone), and that cell phones should not be kept next to the body. Use of wires/cables in schools and homes circumvents needless exposures of children to radiation from both devices and Wi-Fi routers. There is also an urgent need for research to evaluate the risks to the eye from use of cell phones in virtual reality applications.

<https://www.sciencedirect.com/science/article/pii/S0013935118302561>

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Mobile phone types and SAR characteristics of the human brain

Lee AK, Hong SE, Kwon JH, Choi HD, Cardis E. Mobile phone types and SAR characteristics of the human brain. *Phys Med Biol.* 2017 Mar 7;62(7):2741-2761.

Abstract

Mobile phones differ in terms of their operating frequency, outer shape, and form and location of the antennae, all of which affect the spatial distributions of their electromagnetic field and the level of electromagnetic absorption in the human head or brain. For this paper, the specific absorption rate (SAR) was calculated for four anatomical head models at different ages using 11 numerical phone models of different shapes and antenna configurations. The 11 models represent phone types accounting for around 86% of the approximately 1400 commercial phone models released into the Korean market since 2002. Seven of the phone models selected have an internal dual-band antenna, and the remaining four possess an external antenna. Each model was intended to generate an average absorption level equivalent to that of the same type

of commercial phone model operating at the maximum available output power. The 1 g peak spatial SAR and ipsilateral and contralateral brain-averaged SARs were reported for all 11 phone models. The effects of the phone type, phone position, operating frequency, and age of head models on the brain SAR were comprehensively determined.

<https://www.ncbi.nlm.nih.gov/pubmed/28267685>

Excerpts

Both the psSAR in the brain and the brain hemisphere-averaged SAR were analyzed for the four anatomical head models and 11 representative phone models. The head models used are Eartha and Billie (8 and 11 year-old females), and Louis and Duke (14 and 34 year-old males) from IT'IS. The 11 phone models include bar, slider, and flip types operating at 835 and 1850 MHz (1765 MHz for some of the flip-type models)

- Phone positions and SAR. The gap in the psSAR between the cheek and tilt positions is small in the brain compared to that in the SAM phantom. Flip-type phone models with an external antenna (M8h, M8w, M9h, and M9w) generated higher SAR levels at the left position than at the right position for both frequencies.
- Frequency and SAR. Both the psSAR and the brain hemisphere-averaged SAR are higher at low frequency (835 MHz) than at high frequency (1850 or 1765 MHz). This seems to be because the electromagnetic energy penetrates deeper and is deposited in a larger 'hot spot' area at lower frequency.
- Phone types and SAR. ...The closer the antenna is located to the receiver of the phone, the higher the SAR that seems to appear in the brain. The variability in the psSAR in the brain is much higher between the different phone types than between the different head models. It suggests that it is crucial for study subjects to report exact information on the phone models used for proper exposure assessments in epidemiological studies.
- Laterality of brain hemisphere-averaged SAR. The contralateral brain-averaged SAR level of some models such as M7 and M8 at low frequency is comparable to their ipsilateral brain-averaged SAR at high frequency.
- Age-related changes in SAR. Both the psSAR (tables 2 and 3) and the brain hemisphere-averaged SAR (figures 11 and 12) seem to be strongly influenced by the distance between the head (or auricle) surface and the surface of the temporal lobe of the brain; the temporal lobe of Eartha is the farthest away from the phone body out of all of head models, and Eartha showed the lowest 1 g psSAR and lowest ipsilateral brain-averaged SAR for most of the cases considered. Overall, the variability in the brain SAR of the four head models in this study did not form a consistent pattern with age.

It is impossible to obtain the proper amount of global information regarding the outer shape, antenna location, operating frequency, and detailed SAR values because the SAR-compliance process for mobile phones varies by country. The phone models used in this paper cover the phone types of around 86% of all commercial models released onto the Korean market since 2002. The closer the antenna is located to the receiver of the phone, the higher the SAR is generally produced in the human brain. The maximum difference in psSAR in the brain between the numerical phone models amounted to around 12 dB. The results suggest that it is very important for all subjects to report exact information on the phone models they use if accurate exposure levels are to be obtained in epidemiological studies

The issue of whether children are more sensitive to EMF emitted from mobile phones has been a hot topic among many researchers over the past two decades. In this study, a maximum

psSAR variability of 5.6 dB was shown between the four head models, but was not dependent on age. To generate representative head models, the anatomical morphology of the human head at different ages and for both genders is being statistically investigated using MR images of hundreds of Koreans from early childhood to adult. The resultant statistical figures will become the foundation for detecting age-related influences on the SAR.

<http://iopscience.iop.org/article/10.1088/1361-6560/aa5c2d/meta>

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Temperature distribution and Specific Absorption Rate inside a child's head

Stanković V, Jovanović D, Krstić D, Marković V, Cvetković N. Temperature distribution and Specific Absorption Rate inside a child's head. *International Journal of Heat and Mass Transfer*, 2017, 104:559-565.

Highlights

- The numerical analysis of SAR and temperature distribution within a child head.
- Determination of SAR and increasing of temperature within biological tissues.
- Dependence of the SAR and temperature values on the distance.
- Comparison of results obtained by numerical calculation with experimental results.

Abstract

This paper represents the numerical analysis of Specific Absorption Rate (SAR) and temperature distribution within a real child head model exposed to mobile phone radiation at the frequency of $f = 900$ MHz. In this research the SAR and temperature distribution are obtained by numerical solutions of the equation of electromagnetic waves propagation and by bioheat equation, respectively, and are shown inside different biological tissues and organs during exposure to electromagnetic radiation from a mobile phone. As electromagnetic properties of tissues depend on the electromagnetic waves frequency, the value of SAR and temperature will be different for different tissues and organs. The maximum absorption of electromagnetic energy is in the surface layers of the model, whereby this value is greater than the maximum allowed value defined by standards. Furthermore, the increase in temperature is the highest in those biological tissues and organs that are closest to the source of radiation i.e. a mobile phone. Moving away from a mobile phone, the temperature decreases, but more slowly than the SAR values. In the analysis of the temperature rise resulting from tissues and organs heating due to the effects of electromagnetic fields on a child's head, special attention will be given to the maximum temperature increase in the brain.

Conclusion

This study investigated the distribution of SAR and temperature rise in the anatomical model of a child's head exposed to electromagnetic fields from mobile phones. It was determined that although the values of SAR and temperature decrease with the distance from the source of

radiation, it is not possible to establish a direct connection between these quantities. This is primarily because the SAR represents instantaneous heating of tissue. The distribution of temperature will vary compared to the distribution of SAR due to different mechanisms of heat transfer in the thermal model of a child's head.

Although the value of SAR in the brain is below the maximum allowable values, the fact that the SAR levels in certain tissues and organs of the model are significantly above the maximum allowable value must not be disregarded. It is precisely these areas of a child's head that should be the focus of further research of possible unwanted effects of mobile phone radiation.

On the other hand, the temperature of the brain does not exceed 0.7 C, which is below the threshold for causing undesirable thermal effects on neurons [29], while in other parts of the head the temperature does not exceed 1 C.

Of course, it should be noted that the exposure to electromagnetic radiation for 15 min was simulated. Therefore, the obtained results suggest that, in addition to a dosimetry analysis, it is also necessary to perform the thermal analysis of the impact of mobile phone radiation.

<https://www.sciencedirect.com/science/article/pii/S0017931016313849>

3.0. Human Cell Sample (In Vitro) Studies

3.1. Oxidative stress, DNA damage and cancer

Effect of cell-phone RF on angiogenesis and cell invasion in human head and neck cancer cells

Alahmad YM, Aljaber M, Saleh AI, Yalcin HC, Aboukassim T, Yasmeeen A, Batist G, Moustafa AA. Effect of cell-phone radiofrequency on angiogenesis and cell invasion in human head and neck cancer cells. *Head Neck*. 2018 May 13. doi: 10.1002/hed.25210.

Abstract

BACKGROUND: Today, the cell phone is the most widespread technology globally. However, the outcome of cell-phone radiofrequency on head and neck cancer progression has not yet been explored.

METHODS: The chorioallantoic membrane (CAM) and human head and neck cancer cell lines, FaDu and SCC25, were used to explore the outcome of cell-phone radiofrequency on angiogenesis, cell invasion, and colony formation of head and neck cancer cells, respectively. Western blot analysis was used to investigate the impact of the cell phone on the regulation of E-cadherin and Erk1/Erk2 genes.

RESULTS: Our data revealed that cell-phone radiofrequency promotes angiogenesis of the CAM. In addition, the cell phone enhances cell invasion and colony formation of human head and neck cancer cells; this is accompanied by a downregulation of E-cadherin expression. More significantly, we found that the cell phone can activate Erk1/Erk2 in our experimental models.

CONCLUSION: Our investigation reveals that cell-phone radiofrequency could enhance head and neck cancer by stimulating angiogenesis and cell invasion via Erk1/Erk2 activation.

<https://www.ncbi.nlm.nih.gov/pubmed/29756334>

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Oxidative stress response in SH-SY5Y cells exposed to short-term 1800 MHz RF radiation

Marjanovic Cermak AM, Pavicic I, Trosic I. Oxidative stress response in SH-SY5Y cells exposed to short-term 1800 MHz radiofrequency radiation. *J Environ Sci Health A Tox Hazard Subst Environ Eng*. 2018 Jan 28;53(2):132-138. doi: 10.1080/10934529.2017.1383124.

Abstract

The exact mechanism that could explain the effects of radiofrequency (RF) radiation exposure at non-thermal level is still unknown. Increasing evidence suggests a possible involvement of reactive oxygen species (ROS) and development of oxidative stress. To test the proposed

hypothesis, human neuroblastoma cells (SH-SY5Y) were exposed to 1800 MHz short-term RF exposure for 10, 30 and 60 minutes. Electric field strength within Gigahertz Transverse Electromagnetic cell (GTEM) was 30 V m⁻¹ and specific absorption rate (SAR) was calculated to be 1.6 W kg⁻¹. Cellular viability was measured by MTT assay and level of ROS was determined by fluorescent probe 2',7'-dichlorofluorescein diacetate. Concentrations of malondialdehyde and protein carbonyls were used to assess lipid and protein oxidative damage and antioxidant activity was evaluated by measuring concentrations of total glutathione (GSH). After radiation exposure, viability of irradiated cells remained within normal physiological values. Significantly higher ROS level was observed for every radiation exposure time. After 60 min of exposure, the applied radiation caused significant lipid and protein damage. The highest GSH concentration was detected after 10 minute-exposure. The results of our study showed enhanced susceptibility of SH-SY5Y cells for development of oxidative stress even after short-term RF exposure.

<https://www.ncbi.nlm.nih.gov/pubmed/29148897>

3.2. Effects on stem cell growth

Effects of RF-EMF Exposure from GSM Mobile Phones on Proliferation Rate of Human Adipose-derived Stem Cells: An In-vitro Study

Shahbazi-Gahrouei D, Hashemi-Beni B, Ahmadi Z. Effects of RF-EMF Exposure from GSM Mobile Phones on Proliferation Rate of Human Adipose-derived Stem Cells: An In-vitro Study. J Biomed Phys Eng. 2016 Dec 1;6(4):243-252.

Abstract

BACKGROUND: As the use of mobile phones is increasing, public concern about the harmful effects of radiation emitted by these devices is also growing. In addition, protection questions and biological effects are among growing concerns which have remained largely unanswered. Stem cells are useful models to assess the effects of radiofrequency electromagnetic fields (RF-EMF) on other cell lines. Stem cells are undifferentiated biological cells that can differentiate into specialized cells. Adipose tissue represents an abundant and accessible source of adult stem cells. The aim of this study is to investigate the effects of GSM 900 MHz on growth and proliferation of mesenchymal stem cells derived from adipose tissue within the specific distance and intensity.

MATERIALS AND METHODS: ADSCs were exposed to GSM mobile phones 900 MHz with intensity of 354.6 μ W/cm² square waves (217 Hz pulse frequency, 50% duty cycle), during different exposure times ranging from 6 to 21 min/day for 5 days at 20 cm distance from the antenna. MTT assay was used to determine the growth and metabolism of cells and trypan blue test was also done for cell viability. Statistical analyses were carried out using analysis of one way ANOVA. P<0.05 was considered to be statistically significant.

RESULTS: The proliferation rates of human ADSCs in all exposure groups were significantly lower than control groups ($P < 0.05$) except in the group of 6 minutes/day which did not show any significant difference with control groups.

CONCLUSION: The results show that 900 MHz RF signal radiation from antenna can reduce cell viability and proliferation rates of human ADSCs regarding the duration of exposure.

<https://www.ncbi.nlm.nih.gov/pubmed/28144594>

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900 MHz GSM Cell Phone Radiation Alters Human MCF-7 Cells & Stem Cells

Shahbazi-Gahrouei D, Hashemi-Beni B, Moradi A, Aliakbari M, Shahbazi-Gahrouei S. Exposure to Global System for Mobile Communication 900 MHz Cellular Phone Radiofrequency Alters Growth, Proliferation and Morphology of Michigan Cancer Foundation-7 Cells and Mesenchymal Stem Cells. *Int J Prev Med.* 2018; 9: 51. Published online 2018 Jun 19. doi: 10.4103/ijpvm.IJPVM_75_17.

Abstract

Background: Today, using cellular phone and its harmful effects in human life is growing. The aim of this study is to investigate the effect of the global system for mobile communication (GSM) 900 MHz cellular phone radiofrequency waves on growth, morphology, and proliferation rate of mesenchymal stem cells and Michigan Cancer Foundation (MCF-7) cells within the specific distance and intensity.

Methods: MCF-7 and human adipose-derived stem cells (HADSCs) were exposed to GSM cellular phones 900 MHz frequency with intensity of $354.6 \mu\text{W}/\text{cm}^2$ during different exposure times 6, 21, 51, and 101 min/day with an interval of 10 min for each subsequent radiation exposure for 3 and 5 days at 10 and 20 cm distances from antenna. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay and trypan blue test were used to determine the growth of cells and cell viability, respectively. Statistical analyses were carried out using three-way ANOVA. Differences were significant when $P < 0.05$.

Results: The proliferation rates of both MCF-7 and HADSCs cells in all exposure groups were significantly lower than controls ($P < 0.05$). There was a significant effect on the percentage of cell survival with increase the period of time from 3 to 5 days for MCF-7 ($P < 0.01$) and HADSCs ($P = 0.02$), respectively. Variations in distance had no significant effect on the percentage of cell survival ($P = 0.35$) on MCF-7 ($P = 0.02$) and HADSCs ($P = 0.09$) cells, respectively.

Conclusions: The results showed that radiation of GSM 900 MHz cellular phone may be reduced cell viability and proliferation rates of both cells. It is recommended to reduce exposure time, increase distance from antenna, and reserve the use of cell phones for shorter

conversations to prevent its biological and harmful effects. Further studies with other intensities and frequencies on different cells are recommended.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6028991/>

3.3. Reproductive harm

Effects of electromagnetic waves emitted from 3G+wi-fi modems on human semen analysis

Kamali K, Atarod M, Sarhadi S, Nikbakht J, Emami M, Maghsoudi R, Salimi H, Fallahpour B, Kamali N, Momtazan A, Ameli M. Effects of electromagnetic waves emitted from 3G+wi-fi modems on human semen analysis. *Urologia*. 2017 Oct 25;84(4):209-214. doi: 10.5301/uj.5000269.

Abstract

OBJECTIVE: The purpose of this study was to evaluate the effects of 3G+wifi modems on human sperm quality. A total of 40 semen specimens were gathered between March and September 2015, from healthy adult men.

METHODS: The sperm samples were divided into two groups - 3G+wi-fi exposed and unexposed groups. In the unexposed group, the specimens were shielded by aluminum foil in three layers and put into an incubator at a temperature of 37°C for 50 minutes. The exposed group was positioned in another room in an incubator at a temperature of 37°C for 50 minutes. A 3G+wi-fi modem was put into the same incubator and a laptop computer was connected to the modem and was downloading for the entire 50 minutes. Semen analysis was done for each specimen and comparisons between parameters of the two groups were done by using Kolmogorov-Smirnov study and a paired t-test.

RESULTS: Mean percentage of sperm with class A and B motility were not significantly different in two groups ($p = 0.22$ and 0.54 , respectively). In class C, it was significantly lower in the exposed group ($p = 0.046$), while in class D it was significantly higher ($p = 0.022$). Velocity curvilinear, velocity straight line, velocity average path, mean angular displacement, lateral displacement and beat cross frequency were significantly higher in the unexposed group. The limitation was the in vitro design.

CONCLUSIONS: Electromagnetic waves (EMWs) emitted from 3G+wi-fi modems cause a significant decrease in sperm motility and velocity, especially in non-progressive motile sperms. Other parameters of semen analysis did not change significantly. EMWs, which are used in communications worldwide, are a suspected cause of male infertility. Many studies evaluated the effects of cell phones and wi-fi on fertility. To our knowledge, no study has yet been done to show the effects of EMWs emitted from 3G+wi-fi modems on fertility. Our study revealed a

significant decrease in the quality of human semen after exposure to EMWs emitted from 3G+wi-fi modems.

<https://www.ncbi.nlm.nih.gov/pubmed/28967061>

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Cell phone use is associated with an inflammatory cytokine profile of parotid gland saliva

Siqueira EC, de Souza FT, Ferreira E, Souza RP, Macedo SC, Friedman E, Gomez MV, Gomes CC, Gomez RS. Cell phone use is associated with an inflammatory cytokine profile of parotid gland saliva.. J Oral. Pathol Med. 45(9):682-686. 2016.

Abstract

BACKGROUND: There is controversy on the effects of the non-ionizing radiation emitted by cell phones on cellular processes and the impact of such radiation exposure on health. The purpose of this study was to investigate whether cell phone use alters cytokine expression in the saliva produced by the parotid glands.

METHODS: Cytokine expression profile was determined by enzyme linked immuno sorbent assay (ELISA) in the saliva produced by the parotid glands in healthy volunteers, and correlated with self-reported cell phone use and laterality.

RESULTS: The following parameters were determined, in 83 Brazilian individuals in saliva produced by the parotid glands comparing the saliva from the gland exposed to cell phone radiation (ipsilateral) to that from the contralateral parotid: salivary flow, total protein concentration, interleukin 1 β (IL-1 β), interleukin 6 (IL-6), interleukin 10 (IL-10), interferon γ (IFN- γ), and tumor necrosis factor α (TNF- α) salivary levels by ELISA. After multiple testing correction, decreased IL-10 and increased IL-1 β salivary levels in the ipsilateral side compared with the contralateral side ($P < 0.05$) were detected. Subjects who used cell phones for more than 10 years presented higher differences between IL-10 levels in ipsilateral versus contralateral parotids ($P = 0.0012$). No difference was observed in any of the tested parameters in correlation with cell phone monthly usage in minutes.

CONCLUSION: The exposure of parotid glands to cell phones can alter salivary IL-10 and IL-1 β levels, consistent with a pro-inflammatory microenvironment that may be related to heat production.

<http://1.usa.gov/24cKkun>

3.4. Other effects

Effect of RF EMF from mobile phones on nickel release from orthodontic brackets: An in vitro study

Seyed Mohammad S, Mortazavi J, Paknahad M, Khaleghi I, Eghlidospour M. Effect of radiofrequency electromagnetic fields (RF-EMFS) from mobile phones on nickel release from orthodontic brackets: An in vitro study. *International Orthodontics*, Available online 12 July 2018.

Summary

Background The worldwide dramatic increase in the use of cell phones has generated great concerns about their potential adverse health effects.

Objective The aim of the present study was to evaluate the effects of radiofrequency electromagnetic fields (RF-EMFs) emitted from mobile phones on the level of nickel release from orthodontic brackets.

Methods Twenty stainless steel brackets were divided randomly into experimental and control groups (n = 10). Brackets were immersed in artificial saliva at 37 °C for 6 months. Experimental group were exposed to GSM 900 MHz RF-EMFs emitted from a mobile phone stimulator for 4 hours. The specific absorption rate (SAR) was 2.287 W/kg. The concentration of nickel in the artificial saliva in both groups was evaluated by using the cold-vapour atomic absorption spectrometry. The Mann-Whitney test was used to assess significant differences in nickel release between the exposed and non-exposed groups.

Results The mean nickel levels in the exposed and non-exposed groups were 11.95 and 2.89 µg/l, respectively. This difference between the concentrations of nickel in the artificial saliva of these groups was statistically significant (P = 0.001).

Conclusion Exposure to RF-EMFs emitted from mobile phones can lead to human exposure to higher levels of nickel in saliva in patients with orthodontic appliances. As nickel exposure can lead to allergic reaction in humans and considering this point that about 10–20% of the population can be hypersensitive to nickel, further studies are needed to evaluate the effects of radiofrequency electromagnetic fields (RF-EMFs) emitted from common devices such as mobile phones or Wi-Fi routers on the level of nickel release from orthodontic brackets.

<https://www.sciencedirect.com/science/article/pii/S1761722718300962?via%3Dihub>

4.0. Live (in vivo) Animal Studies

4.1. National Toxicology Program: Genotoxic effects and cancer studies

Guidry V. "NTP cell phone studies—experts recommend elevated conclusions." Environmental factor: Your online source for NIEHS news. National Institute of Environmental Health Sciences. April, 2018. (news report)

A panel of external scientific experts met March 26-28 at NIEHS and [recommended](#) that some National Toxicology Program (NTP) conclusions be changed to indicate stronger levels of evidence that cell phone radiofrequency radiation (RFR) caused tumors in rats.

The panel agreed with NTP conclusions that there was little indication of RFR-related health problems in mice. The panel reviewed the conclusions of two draft [technical reports](#), one in rats and one in mice, based on 10 years and \$25 million of research.

"It was gratifying that the members of the expert panel unanimously praised the NTP cell phone studies as very well done, and vitally important research," said NTP Senior Scientist John Bucher, Ph.D. "They conducted a thorough review, engaged in spirited debate, and grappled with the same uncertainties as did the NTP staff."

Bucher stressed that the goal of the study was to establish the potential health hazard of exposure to cell phone RFR. He said that to detect a potential effect, the rodents' whole bodies were exposed to levels equal to and higher than the highest level permitted for local tissue exposure in cell phone emissions today.

[Heart, brain, and adrenal tumors](#)

Working from the NTP scale of clear evidence, some evidence, equivocal evidence, and no evidence, the panel made several recommendations.

The experts recommended that tumors in tissues surrounding nerves in the hearts of male rats, called malignant schwannomas, be reclassified from some evidence to clear evidence of carcinogenic activity.

In female rats, they recommended reclassification of malignant schwannomas from no evidence to equivocal evidence of carcinogenic activity. The panel agreed that there were unusual patterns of cardiomyopathy, or damage to heart tissue, in exposed male and female rats.

"When I look at these types of studies, I look for high-level signals that can infer mechanisms. I have more questions than answers, but the heart is clearly sending a signal in the rat studies, between the levels of cardiomyopathy and malignant tumors," said panelist Rick Adler, D.V.M., Ph.D., senior director of discovery and regulatory pathology for GlaxoSmithKline.

The panel recommended that findings for a type of brain tumor, called malignant glioma, and a tumor in the adrenal gland, called pheochromocytoma, be reclassified as some evidence of carcinogenic activity in male rats.

[Tissue changes and lower body weights](#)

NTP researchers also looked for noncancerous health effects in rats and mice. The panel agreed that there were increases in damage to brain tissue in exposed male and female rats, which further supported the classifications of cancerous effects in the brain.

For several other tissues, including the prostate and pituitary glands, the panel agreed that tissue changes were equivocal, meaning it was unclear if any of these tumor increases were related to RFR.

NTP also reported lower body weights among newborn rats and their mothers, especially when exposed to high levels of RFR during pregnancy and lactation, but these animals later grew to normal size.

“I want to highlight that we don’t rely on one specific item for determining response,” said NTP toxicologist Chad Blystone, Ph.D. He explained that NTP staff review numerous factors when determining conclusions, including those listed below.

- Statistics.
- Dose-response relationship.
- Commonality of tumors and tissue changes.
- Comparison to concurrent and historical controls.
- Findings across sexes and species.

Most expensive, technically challenging studies

To conduct the studies, NTP worked with collaborators at the [IT’IS Foundation](#) to design special chambers that exposed rats and mice to different levels of RFR for up to two years, including exposure to pups while in the womb.

Myles Capstick, Ph.D., of the IT’IS Foundation explained that they wanted to expose the whole animals because they were not sure where health effects might occur. “We were aiming to expose as many tissues as possible, not mimic a phone next to the head,” said Capstick.

Exposure levels ranged from 1.5 to 6 watts per kilogram in rats and 2.5 to 10 watts per kilogram in mice. The low power level for rats was equal to the highest level permitted for local tissue exposures to cell phone emissions today. The animals were exposed for 10-minute on, 10-minute off cycles that totaled more than 9 hours each day.

The studies used 2G and 3G frequencies and modulations that are still used in voice calls and texting in the United States. More recent 4G, 4G-LTE, and 5G networks for streaming video and downloading attachments use different cell phone signal frequencies and modulations than NTP used in these studies. Niels Kuster, Ph.D., of the IT’IS Foundation added that their studies of 4G technologies are very similar.

There were approximately 3,000 animals in the study, and pathologists examined 50 tissues in each animal to look for signs of cancer or other changes.

<https://factor.niehs.nih.gov/2018/4/feature/feature-2-cell-phone/index.htm>

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NTP Technical Report on the Toxicology & Carcinogenesis Studies in Rats Exposed to Whole-Body Radio Frequency Radiation Used by Cell Phones

National Toxicology Program. NTP Technical Report on the Toxicology and Carcinogenesis Studies in Hsd:Sprague Dawley SD Rats Exposed to Whole-Body Radio Frequency Radiation at a Frequency (900 MHz) and Modulations (GSM and CDMA) Used by Cell Phones. Peer review draft.2018. NTP TR 595. NIEHS, NIH, US DHHS.

ABSTRACT

GSM- AND CDMA-MODULATED CELL PHONE RADIO FREQUENCY RADIATION

The predominant source of human exposure to radio frequency radiation (RFR) occurs through the use of cellular phone handsets. The Food and Drug Administration nominated cell phone RFR emission for toxicology and carcinogenicity testing in 1999. At that time, animal experiments were deemed crucial because meaningful human exposure data from epidemiological studies were not available. Male and female Hsd:Sprague Dawley SD rats were exposed to time-averaged whole-body specific absorption rates of Global System for Mobile Communications (GSM)- or Code Division Multiple Access (CDMA)-modulated cell phone RFR at frequencies of 900 MHz (herein referred to as “cell phone RFR”) *in utero*, during lactation, and after weaning for 28 days or 2 years. Genetic toxicology studies were conducted in rat peripheral blood erythrocytes and leukocytes, brain cells, and liver cells.

STUDY DESIGN

28-Day Studies

Beginning on gestation day (GD) 6, groups of 20 time-mated F0 female rats were housed in specially-designed reverberation chambers and received whole-body exposures to GSM- or CDMA-modulated cell phone RFR at power levels of 0 (sham control), 3, 6 or 9 W/kg for 5 to 7 days per week, continuing throughout gestation and lactation. The daily exposure duration was 9 hours and 10 minutes over an 18-hour and 20-minute period, as exposures cycled between modulations every 10 minutes. There were seven exposure groups per sex, including a shared sham control and three exposure groups for each modulation. At weaning, 10 males and 10 females per group were selected across four litters for continuation. Weaning occurred on the day the last litter reached postnatal day (PND) 21, marking the beginning of the 28-day study. Male and female F1 offspring continued to receive whole-body exposures to GSM- or CDMA-modulated cell phone RFR at the same power levels and under the same exposure paradigm, 5 to 7 days per week for up to 28 days.

2-Year Studies

Beginning on GD 5, groups of 56 time-mated F0 female rats were housed in reverberation chambers and received whole-body exposures to GSM- or CDMA-modulated cell phone RFR at power levels of 0 (sham control), 1.5, 3, or 6 W/kg for 7 days per week, continuing throughout gestation and lactation. The daily exposure duration was 9 hours and 10 minutes over an 18-hour and 20-minute period, as exposures cycled between modulations every 10 minutes. There were seven exposure groups per sex, including a shared sham control and three exposure groups for each modulation. At weaning, three males and three females per litter from 35 litters were randomly selected per exposure group for continuation. Weaning occurred on the

day the last litter reached PND 21, marking the beginning of the 2-year studies. Groups of 105 male and 105 female F1 offspring continued to receive whole-body exposures to GSM- or CDMA-modulated cell phone RFR at the same power levels and under the same exposure paradigm, 7 days per week for up to 104 weeks. After 14 weeks of exposure, 10 rats per group were randomly selected for interim histopathologic evaluation and five were designated for genetic toxicity evaluation.

PERINATAL FINDINGS AND THERMAL EFFECTS

Consistent perinatal effects were observed between modulations, and in both the 28-day and 2-year studies, including lower dam body weights in late gestation and lactation, lower pup body weights and lower pup survival rates. Whole-body exposure to GSM- or CDMA-modulated cell phone RFR had no effect on survival of dams during gestation or lactation and no effect on littering, litter size or live litter pup numbers on PND 1. Lower body weight gains were observed during gestation in dams exposed to GSM during the 28-day and 2-year studies and the CDMA 28-day studies, with body weight effects becoming more pronounced and persisting throughout lactation for both modulations and studies. Lower pup survival was observed for GSM exposure at 9 W/kg in early lactation (before PND 4) and at 6 and 9 W/kg in CDMA-exposed animals, in early and late (after PND 4) lactation. Lower male and female pup body weights were observed beginning in early lactation following exposure to ≥ 6 W/kg of either GSM- or CDMA-modulated cell phone RFR.

Body weight decreases in RFR exposed groups persisted throughout the post-weaning period in the 28-day studies, were observed at the 14-week interim evaluation in the 2-year studies, but eventually resolved and were not observed at later time points in the 2-year studies. There were no clinical observations associated with exposures to either modulation.

In the 28-day studies, subcutaneously implanted microchips were used to record body temperatures of animals within 3 to 5 minutes of exposure pauses. Body temperatures were recorded in F0 females during gestation and lactation and in F1 offspring during the post-weaning phase. Higher body temperatures were observed during gestation in 9 W/kg GSM dams and during lactation in ≥ 6 W/kg GSM dams and 9 W/kg CDMA dams. At power levels selected for the 2-year studies (up to 6 W/kg), body temperature elevations did not exceed 1° C in the 28-day study measurements. No exposure-related temperature effects were observed in F1 offspring.

2-Year Studies

In the 2-year studies, there was significantly lower survival in the shared male sham control group compared to almost all exposed groups, for both modulations. Survival began to decline at a faster rate than in exposed groups after week 75. In the sham control group, 28% of animals survived to study termination, compared to 48% to 68% for exposed groups across both modulations. Lower survival in sham control male rats was largely attributed to higher severity of chronic progressive nephropathy and there was a spectrum of lesions in other organs considered secondary to chronic progressive nephropathy that occurred at higher incidences in male sham controls. Survival in the shared female sham control group was significantly lower than the 6 W/kg CDMA-exposed group; however, it was similar to all other exposure groups, across modulations. At study termination, there was no effect on body weight in male or female rats, and there were no exposure-related clinical observations.

At the 14-week interim evaluation, there were increased incidences of right ventricular cardiomyopathy in the heart of male rats following exposure to GSM- and CDMA-modulated cell phone RFR compared to sham controls.

At 14 weeks, sperm motility and counts were evaluated in male rats exposed to GSM or CDMA. Exposure to whole-body GSM- or CDMA-modulated cell phone RFR, up to 6 W/kg, did not result in significant changes/differences in reproductive organ histopathology or sperm parameters in male rats compared to the sham controls.

At 2 years, there were similarities in neoplastic and nonneoplastic responses between modulations. Following exposure to GSM- or CDMA-modulated cell phone RFR, there were increases in the incidences of malignant schwannoma in the heart of male rats, with a significant positive trend in the incidences in GSM- and CDMA-exposed males and a significant pairwise increased incidence in CDMA 6 W/kg males. Also observed in the heart were significantly increased incidences of right ventricular cardiomyopathy in 3 and 6 W/kg GSM male and female rats and 6 W/kg CDMA male rats.

Several other, weaker, responses were observed in both modulations including malignant glioma in the brain, adenomas in the pituitary gland (pars distalis), and pheochromocytomas of the adrenal medulla. Additionally, in GSM male rats there were marginal responses in the prostate gland, granular cell tumors of the brain, and in pancreatic islets that were not observed in CDMA-exposed rats, and in CDMA-exposed male rats, there was a response in the liver. The relationship between these responses and exposure to GSM or CDMA RFR was uncertain.

In the brain, there were incidences (not statistically significant) of malignant glioma in all groups of GSM male rats, in 6 W/kg CDMA male rats, and in 1.5 W/kg CDMA females, compared to no incidences in either the male or female sham control groups. There were also occurrences of glial cell hyperplasia in the brain of GSM and CDMA male rats and CDMA female rats that were not observed in sham control animals.

In the pituitary gland (pars distalis) of male rats, there were increased (not statistically significant) incidences of adenoma in all GSM-exposed groups and significantly increased incidences in 3 W/kg CDMA males compared to the sham controls.

There were significantly increased incidences of benign, malignant or complex pheochromocytoma (combined) in the adrenal medulla of the 1.5 and 3 W/kg GSM male rats and 1.5 W/kg CDMA female rats. In GSM female rats, there were increased incidences of hyperplasia in the adrenal medulla at 6 W/kg.

There were increased incidences (not statistically significant) of prostate gland adenoma in 3 W/kg rats, and a single incidence of prostate gland carcinoma in the same group. The incidence and severity of prostate epithelial hyperplasia was slightly higher in all exposed groups of GSM male rats. An exposure-related increase in the incidence of prostate gland epithelial hyperplasia was also observed in CDMA male rats.

There were increased incidences (not statistically significant) of benign granular cell tumor in the brain of all exposed groups of GSM male rats compared to the sham controls, and a single incidence of malignant granular cell tumor in the 3 W/kg GSM group.

There was a significantly increased incidence of adenoma or carcinoma (combined) in pancreatic islets in 1.5 W/kg GSM male rats.

In CDMA male rats, there were incidences of hepatocellular adenoma in all exposed groups, and one incidence of carcinoma each in the 3 and 6 W/kg groups. These neoplasms were not statistically significant, but were not observed in the sham control group.

A few nonneoplastic lesions that were not associated with any of the neoplastic responses were also observed. There were increased incidences of thyroid gland C-cell hyperplasia in all groups of GSM-exposed female rats.

Genetic Toxicology

As part of the 14-week interim evaluation, samples of frontal cortex, hippocampus, cerebellum, liver, and blood leukocytes were evaluated for DNA damage using the comet assay (two sexes, two cell phone RFR modulations, and five tissues per animal). Samples of peripheral blood were also evaluated for chromosome damage in the micronucleus assay. Results are based on the 100-cell scoring approach that was standard at the time of the studies; data obtained using a second, 150-cell scoring approach recommended in a recently adopted international guideline for the *in vivo* comet assay, are noted for the few instances where results differed between the two methods. A significant increase in DNA damage (% tail DNA) was observed in hippocampus cells of male rats exposed to the CDMA modulation. Although the levels of DNA damage in hippocampus cells were also increased in an exposure related fashion using the 150-cell scoring approach, the increases were not statistically significant. An exposure-related increase in DNA damage seen in the cells of the frontal cortex of male rats exposed to the CDMA modulation was judged to be equivocal based on a significant trend test. Although results from scoring 100 cells were negative for male rat blood leukocytes exposed to either CDMA or GSM modulations, the results (both CDMA and GSM) were judged to be equivocal when evaluated using the 150-cell scoring method. No statistically significant increases in DNA damage were observed in any of the female rat samples scored with the 100-cell approach; with the 150-cell approach, results in peripheral blood leukocytes of female rats (CDMA) were judged to be equivocal.

No significant increases in micronucleated red blood cells or changes in the percentage of immature erythrocytes among total erythrocytes were observed in peripheral blood of rats of either sex exposed to either modulation of cell phone RFR.

Conclusions

Under the conditions of this 2-year whole-body exposure study, there was *some evidence of carcinogenic activity* of GSM-modulated cell phone RFR at 900 MHz in male Hsd:Sprague Dawley SD rats based on the incidences of malignant schwannoma in the heart. The incidences of adenoma or carcinoma (combined) in the prostate gland, malignant glioma and benign or malignant granular cell tumors in the brain, adenoma of the pars distalis in the pituitary gland, pheochromocytoma (benign, malignant, or complex combined) in the adrenal medulla, and pancreatic islet cell adenoma or carcinoma (combined) may have been related to cell phone RFR exposure. There was *no evidence of carcinogenic activity* of GSM-modulated cell phone RFR at 900 MHz in female Hsd:Sprague Dawley SD rats administered 1.5, 3, or 6 W/kg. There was *some evidence of carcinogenic activity* of CDMA-modulated cell phone RFR at 900 MHz in male Hsd:Sprague Dawley SD rats based on the incidences of malignant schwannoma in the heart. The incidences of malignant glioma in the brain, adenoma of the pars distalis in the pituitary gland, and adenoma or carcinoma (combined) of the liver may have been related to cell phone RFR exposure. There was *equivocal evidence of carcinogenic activity* of CDMA-modulated cell phone RFR at 900 MHz in female Hsd:Sprague Dawley SD rats based on the

incidences of malignant glioma in the brain and pheochromocytoma (benign, malignant, or complex combined) in the adrenal medulla.

Increases in nonneoplastic lesions in the heart, brain, and prostate gland of male rats, and of the heart, thyroid gland, and adrenal gland in female rats occurred with exposures to GSM cell phone RFR at 900 MHz. Increases in nonneoplastic lesions of the heart, brain, and prostate gland occurred in males, and of the brain in females exposed to CDMA cell phone RFR at 900 MHz.

https://ntp.niehs.nih.gov/ntp/about_ntp/trpanel/2018/march/tr595peerdraft.pdf

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Report of partial findings from the NTP Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in rats

Wyde M, Cesta M, Blystone C, Elmore S, Foster P, Hooth M, Kissling G, Malarkey D, Sills R, Stout M, Walker N, Witt K, Wolfe M, Bucher J. Report of Partial findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats (Whole Body Exposure). Draft published online Feb 1, 2018. doi: <https://doi.org/10.1101/055699>.

Abstract

The U.S. National Toxicology Program (NTP) has carried out extensive rodent toxicology and carcinogenesis studies of radiofrequency radiation (RFR) at frequencies and modulations used in the U.S. telecommunications industry. This report presents partial findings from these studies. The occurrences of two tumor types in male Harlan Sprague Dawley rats exposed to RFR, malignant gliomas in the brain and schwannomas of the heart, were considered of particular interest and are the subject of this report. The findings in this report were reviewed by expert peer reviewers selected by the NTP and National Institutes of Health (NIH). These reviews and responses to comments are included as appendices to this report, and revisions to the current document have incorporated and addressed these comments. When the studies are completed, they will undergo additional peer review before publication in full as part of the NTP's Toxicology and Carcinogenesis Technical Reports Series. No portion of this work has been submitted for publication in a scientific journal. Supplemental information in the form of four additional manuscripts has or will soon be submitted for publication. These manuscripts describe in detail the designs and performance of the RFR exposure system, the dosimetry of RFR exposures in rats and mice, the results to a series of pilot studies establishing the ability of the animals to thermoregulate during RFR exposures, and studies of DNA damage. (1) Capstick M, Kuster N, Kuhn S, Berdinas-Torres V, Wilson P, Ladbury J, Koepke G, McCormick D, Gauger J, and Melnick R. A radio frequency radiation reverberation chamber exposure system for rodents; (2) Yijian G, Capstick M, McCormick D, Gauger J, Horn T, Wilson P, Melnick RL, and Kuster N. Life time dosimetric assessment for mice and rats exposed to cell phone radiation; (3) Wyde ME, Horn TL, Capstick M, Ladbury J, Koepke G, Wilson P, Stout MD, Kuster N, Melnick R, Bucher JR, and McCormick D. Pilot studies of the National Toxicology Program's cell phone radiofrequency radiation reverberation chamber exposure system; (4) Smith-Roe SL, Wyde ME,

Stout MD, Winters J, Hobbs CA, Shepard KG, Green A, Kissling GE, Tice RR, Bucher JR, and Witt KL. Evaluation of the genotoxicity of cell phone radiofrequency radiation in male and female rats and mice following subchronic exposure.

Open access paper: <https://www.biorxiv.org/content/early/2018/02/01/055699>

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NTP Technical Report on the Toxicology & Carcinogenesis Studies in Mice Exposed to Whole-Body Radio Frequency Radiation Used by Cell Phones

National Toxicology Program. NTP Technical Report on the Toxicology and Carcinogenesis Studies in B6C3F1/N Mice Exposed to Whole-Body Radio Frequency Radiation at a Frequency (1900 MHz) and Modulations (GSM and CDMA) Used by Cell Phones. Peer review draft. 2018. NTP TR 596. NIEHS, NIH, US DHHS.

GSM- AND CDMA-MODULATED CELL PHONE RADIO FREQUENCY RADIATION

The predominant source of human exposure to radio frequency radiation (RFR) occurs through usage of cellular phone handsets. The Food and Drug Administration nominated cell phone RFR emission for toxicology and carcinogenicity testing in 1999. At that time, animal experiments were deemed crucial because meaningful human exposure data from epidemiological studies were not available. Male and female B6C3F1/N mice were exposed to time-averaged whole-body specific absorption rates of 0 (sham control), 5, 10, or 15 W/kg Global System for Mobile Communications (GSM)- or Code Division Multiple Access (CDMA)-modulated cell phone RFR at 1,900 MHz for 28 days or 0, 2.5, 5, or 10 W/kg GSM- or CDMA-modulated cell phone RFR for up to 2 years. Genetic toxicology studies were conducted in mouse peripheral blood erythrocytes and leukocytes, brain cells, and liver cells.

GSM 28-DAY STUDY

Groups of 10 male and 10 female core study mice and groups of 20 male and 20 female special study mice were housed in specially designed reverberation chambers and received whole-body exposures to GSM-modulated cell phone RFR at power levels of 0 (sham control), 5, 10, or 15 W/kg, for up to 18 hours and 20 minutes per day, 5 or 7 (last week of study) days per week for at least 28 days with continuous cycling of 10 minutes on and 10 minutes off during the exposure periods. The sham control animals were housed in reverberation chambers identical to those used for the exposed groups, but were not exposed to cell phone RFR; a shared group of unexposed mice of each sex served as sham controls for both cell phone RFR modulations. All mice survived to the end of the study. Mean body weights of exposed groups of males and females were similar to controls. There were no exposure-related clinical signs, differences in organ weights, or histopathologic findings. Differences in body temperatures between the exposed groups and the control group were not considered to be related to cell phone RFR exposure.

2-YEAR STUDY

Groups of 105 male and 105 female mice were housed in reverberation chambers and received whole-body exposures to GSM-modulated cell phone RFR at power levels of 0 (sham control), 2.5, 5, or 10 W/kg, 9 hours and 10 minutes per day, 7 days per week for 106 (males) or 108

(females) weeks with continuous cycling of 10 minutes on and 10 minutes off during a period of 18 hours and 20 minutes each day. The sham control animals were housed in reverberation chambers identical to those used for the exposed groups, but were not exposed to cell phone RFR; shared groups of unexposed mice of each sex served as sham controls for both cell phone RFR modulations. Fifteen mice per group were randomly selected from the core group after 10 weeks of study; ten of those 15 mice per group were used for interim evaluation at 14 weeks, and five mice per group were used for genetic toxicity testing at 14 weeks. The remaining 90 animals per group were exposed up to 2 years.

At the 14-week interim evaluation in the 2-year study, mean body weights of exposed groups of males and females were similar to those of the sham controls. There were no changes to the hematology variables attributable to GSM cell phone RFR exposure. Differences in organ weights were not associated with histopathologic findings and were not considered related to exposure. In males, there were no exposure-related effects on reproductive organ weights, testis spermatid concentrations, caudal epididymal sperm concentrations, or sperm motility. In females, there were no exposure related effects on estrous cycle length, number of cycling females, or relative amount of time spent in the estrous stages. The only histopathologic finding at the 14-week interim evaluation was an increased incidence of minimal focal inflammation in the liver of the 5 W/kg males.

In the 2-year study, percent survival was significantly higher for the 5 W/kg males than the sham control group. Survival of the other exposed groups of males and females was generally similar to that of the sham controls. Mean body weights of exposed groups of males and females were similar to those of the sham controls throughout the study.

The combined incidences of fibrosarcoma, sarcoma, or malignant fibrous histiocytoma of the skin were increased in 5 and 10 W/kg males, although not significantly or in an exposure concentration-related manner; however, the incidences exceeded the overall historical control ranges for malignant fibrous histiocytoma. In the lung, there was a significant positive trend in the incidences of alveolar/bronchiolar adenoma or carcinoma (combined) in males. Compared to the sham controls, all exposed groups of females had increased incidences of malignant lymphoma and the incidences in the 2.5 and 5 W/kg groups were significantly increased. The sham control group had a low incidence of malignant lymphoma compared to the range seen in historical controls.

There were no nonneoplastic lesions that were considered related to exposure to GSM-modulated cell phone RFR.

CDMA

28-DAY STUDY

Groups of 10 male and 10 female core study mice and groups of 20 male and 20 female special study mice were housed in reverberation chambers and received whole-body exposures to CDMA-modulated cell phone RFR at power levels of 0 (sham control), 5, 10, or 15 W/kg, for up to 18 hours and 20 minutes per day, 5 or 7 (last week of study) days per week for at least 28 days with continuous cycling of 10 minutes on and 10 minutes off during the exposure periods. The sham control animals were housed in reverberation chambers identical to those used for the exposed groups, but were not exposed to cell phone RFR; a shared group of unexposed mice of each sex served as sham controls for both cell phone RFR modulations. All mice survived to the end of the study. Mean body weights of exposed groups of males and females

were similar to controls. There were no exposure-related clinical signs, differences in organ weights, or histopathologic findings. Differences in body temperatures between the exposed groups and the control group were not considered to be related to cell phone RFR exposure.

2-YEAR STUDY

Groups of 105 male and 105 female mice were housed in reverberation chambers and received whole-body exposures to CDMA-modulated cell phone RFR at power levels of 0 (sham control), 2.5, 5, or 10 W/kg, 9 hours and 10 minutes per day, 7 days per week for 106 (males) or 108 (females) weeks with continuous cycling of 10 minutes on and 10 minutes off during a period of 18 hours and 20 minutes each day. The sham control animals were housed in reverberation chambers identical to those used for the exposed groups, but were not exposed to cell phone RFR; shared groups of unexposed mice of each sex served as sham controls for both cell phone RFR modulations. Fifteen mice per group were randomly selected from the core group after 10 weeks of study; ten of those 15 mice per group were used for interim evaluation at 14 weeks, and five mice per group were used for genetic toxicity testing at 14 weeks. The remaining 90 animals per group were exposed up to 2 years.

At the 14-week interim evaluation of the 2-year study, mean body weights of exposed groups of males and females were similar to those of the sham controls. There were no changes to the hematology variables attributable to CDMA cell phone RFR exposure. Differences in organ weights in male mice were not associated with histopathologic findings and were not considered related to exposure; there were no significant changes in organ weights in females. In males, there were no exposure-related effects on reproductive organ weights, testis spermatid concentrations, caudal epididymal sperm concentrations, or sperm motility. In females, there were no exposure related effects on estrous cyclicity. Compared to the sham controls, there were statistically significant differences for extended estrous in the 2.5 W/kg group and extended diestrus in the 5 W/kg group; however, these changes were considered sporadic due to the lack of an exposure-related response. In the kidney of 10 W/kg females, there was a significantly increased incidence of minimal to mild interstitial lymphocytic cellular infiltration. Percent survival was significantly higher in 2.5 W/kg males compared to that in the sham controls in the 2-year study. Survival of males and females in all other exposed groups was generally similar to that of the sham controls. Mean body weights of exposed groups of males and females were similar to those of the sham controls throughout the study.

There was a significantly increased incidence of hepatoblastoma in 5 W/kg males. Compared to the sham controls, the incidences of malignant lymphoma were increased in all exposed groups of females, and the increase was significant in the 2.5 W/kg group. As noted for the GSM study, the shared sham control group had a low incidence of malignant lymphoma compared to the range observed in historical controls.

There were no nonneoplastic lesions that were considered related to exposure to CDMA-modulated cell phone RFR.

GENETIC TOXICOLOGY

Comet Assay

As part of the 14-week interim evaluation, samples of frontal cortex, hippocampus, cerebellum, liver, and blood leukocytes were evaluated for DNA damage using the comet assay (two sexes,

two cell phone RFR modulations, and five tissues per animal). Samples of peripheral blood were also evaluated for chromosome damage in the micronucleus assay. Results are based on the 100-cell scoring approach that was standard at the time of the study; data obtained using a second 150-cell scoring approach, recommended in a recently adopted international guideline for the *in vivo* comet assay, are noted for the few instances where results differed between the two methods. Significant increases in DNA damage were observed in cells of the frontal cortex of male mice exposed to both modulations, GSM and CDMA. No other tissues showed evidence of a treatment-related effect in male mice. In female mice exposed to the CDMA modulation, significant increases in DNA damage were seen in blood leukocytes at all three exposure levels using both scoring approaches. No statistically significant increases in percent comet tail DNA were observed in any of the samples from female mice exposed to the GSM modulation with the 100-cell scoring method. Scoring 150 cells resulted in an equivocal response in liver of female mice exposed to CDMA; a similar pattern of response was seen with the 100-cell scoring method, but none of the increases were significant.

Micronucleus Assay

No significant increases in micronucleated red blood cells or changes in the percentage of immature erythrocytes among total erythrocytes were observed in the peripheral blood of mice of either sex exposed to either modulation of cell phone RFR.

CONCLUSIONS

Under the conditions of these 2-year studies, there was *equivocal evidence of carcinogenic activity* of GSM-modulated cell phone RFR at 1,900 MHz in male B6C3F1/N mice based on the combined incidences of fibrosarcoma, sarcoma, or malignant fibrous histiocytoma in the skin and the incidences of alveolar/bronchiolar adenoma or carcinoma (combined) in the lung. There was *equivocal evidence of carcinogenic activity* of GSM-modulated cell phone RFR at 1,900 MHz in female B6C3F1/N mice based on the incidences of malignant lymphoma (all organs). There was *equivocal evidence of carcinogenic activity* of CDMA-modulated cell phone RFR at 1,900 MHz in male B6C3F1/N mice based on the incidences of hepatoblastoma of the liver. There was *equivocal evidence of carcinogenic activity* of CDMA-modulated cell phone RFR at 1,900 MHz in female B6C3F1/N mice based on the incidences of malignant lymphoma (all organs).

Exposure to GSM- or CDMA-modulated cell phone RFR at 1,900 MHz did not increase the incidence of any nonneoplastic lesions in male or female B6C3F1/N mice.

Open access paper:

https://ntp.niehs.nih.gov/ntp/about_ntp/trpanel/2018/march/tr596peerdraft.pdf

4.2. Other studies on oxidative stress, genotoxic effects, and cancer

Final results regarding brain & heart tumors in rats exposed from prenatal life until natural death to mobile phone RF (1.8 GHz GSM base station environmental emission)

Falcioni L, Bua L, Tibaldi E, Lauriola M, De Angelis L, Gnudi F, Mandrioli D, Manservigi M, Manservigi F, Manzoli I, Menghetti I, Montella R, Panzacchi S, Sgargi D, Strollo V, Vornoli A,

Belpoggi F. Report of final results regarding brain and heart tumors in Sprague-Dawley rats exposed from prenatal life until natural death to mobile phone radiofrequency field representative of a 1.8 GHz GSM base station environmental emission. *Environ Res.* 2018 Aug;165:496-503. doi: 10.1016/j.envres.2018.01.037.

Abstract

Background: In 2011, IARC classified radiofrequency radiation (RFR) as possible human carcinogen (Group 2B). According to IARC, animals studies, as well as epidemiological ones, showed limited evidence of carcinogenicity. In 2016, the NTP published the first results of its long-term bioassays on near field RFR, reporting increased incidence of malignant glial tumors of the brain and heart Schwannoma in rats exposed to GSM – and CDMA –modulated cell phone RFR. The tumors observed in the NTP study are of the type similar to the ones observed in some epidemiological studies of cell phone users.

Objectives: The Ramazzini Institute (RI) performed a life-span carcinogenic study on Sprague-Dawley rats to evaluate the carcinogenic effects of RFR in the situation of far field, reproducing the environmental exposure to RFR generated by 1.8 GHz GSM antenna of the radio base stations of mobile phone. This is the largest long-term study ever performed in rats on the health effects of RFR, including 2448 animals. In this article, we reported the final results regarding brain and heart tumors.

Methods: Male and female Sprague-Dawley rats were exposed from prenatal life until natural death to a 1.8 GHz GSM far field of 0, 5, 25, 50 V/m with a whole-body exposure for 19 h/day.

Results: A statistically significant increase in the incidence of heart Schwannomas was observed in treated male rats at the highest dose (50 V/m). Furthermore, an increase in the incidence of heart Schwann cells hyperplasia was observed in treated male and female rats at the highest dose (50 V/m), although this was not statistically significant. An increase in the incidence of malignant glial tumors was observed in treated female rats at the highest dose (50 V/m), although not statistically significant.

Conclusions: The RI findings on far field exposure to RFR are consistent with and reinforce the results of the NTP study on near field exposure, as both reported an increase in the incidence of tumors of the brain and heart in RFR-exposed Sprague-Dawley rats. These tumors are of the same histotype of those observed in some epidemiological studies on cell phone users. These experimental studies provide sufficient evidence to call for the reevaluation of IARC conclusions regarding the carcinogenic potential of RFR in humans.

Among male rats, the incidence of heart schwannoma and hyperplasia was 0.7% (3 of 412) in the control group, 1.2% (5/401) in the 5 volts/meter (V/m) group, 1.0% (2/209) in the 25 V/m group, and 3.9% (8/207) in the 50 V/m group. The 50 V/m group had significantly greater incidence than the control group ($p < .02$).

Among male rats, the incidence of glioma and glial cell hyperplasia in the control group was 0.0% (0 of 412), 0.7% (3/401) in the 5 volts/meter (V/m) group, 1.4% (3/209) in the 25 V/m group, and 0.0% (0/207) in the 50 V/m group.

<https://www.ncbi.nlm.nih.gov/pubmed/29530389>

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Cellular stress & caspase-3 resulting from combined two-frequency signal in brains of Sprague-Dawley rats

López-Furelos A, Leiro-Vidal JM, Salas-Sánchez AÁ, Ares-Pena FJ, López-Martín ME. Evidence of cellular stress and caspase-3 resulting from a combined two-frequency signal in the cerebrum and cerebellum of sprague-dawley rats. *Oncotarget*. 2016 Oct 4;7(40):64674-64689. doi: 10.18632/oncotarget.11753.

Abstract

Multiple simultaneous exposures to electromagnetic signals induced adjustments in mammal nervous systems. In this study, we investigated the non-thermal SAR (Specific Absorption Rate) in the cerebral or cerebellar hemispheres of rats exposed in vivo to combined electromagnetic field (EMF) signals at 900 and 2450 MHz. Forty rats divided into four groups of 10 were individually exposed or not exposed to radiation in a GTEM chamber for one or two hours. After radiation, we used the Chemiluminescent Enzyme-Linked Immunosorbent Assay (ChELISA) technique to measure cellular stress levels, indicated by the presence of heat shock proteins (HSP) 90 and 70, as well as caspase-3-dependent pre-apoptotic activity in left and right cerebral and cerebellar hemispheres of Sprague Dawley rats. Twenty-four hours after exposure to combined or single radiation, significant differences were evident in HSP 90 and 70 but not in caspase 3 levels between the hemispheres of the cerebral cortex at high SAR levels. In the cerebellar hemispheres, groups exposed to a single radiofrequency (RF) and high SAR showed significant differences in HSP 90, 70 and caspase-3 levels compared to control animals. The absorbed energy and/or biological effects of combined signals were not additive, suggesting that multiple signals act on nervous tissue by a different mechanism.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5323107/>

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Biochemical & pathological changes in male rat kidney & bladder following exposure to continuous 900-MHz EMF on postnatal days 22-59

Türedi S, Kerimoğlu G, Mercantepe T, Odacı E. Biochemical and pathological changes in the male rat kidney and bladder following exposure to continuous 900-MHz electromagnetic field on postnatal days 22-59. *Int J Radiat Biol*. 2017 Sep;93(9):990-999. doi: 10.1080/09553002.2017.1350768.

Abstract

PURPOSE: To investigate the effect on male rat kidney and bladder tissues of exposure to 900-megahertz (MHz) electromagnetic field (EMF) applied on postnatal days 22-59, inclusive.

MATERIALS AND METHODS: Twenty-four male Sprague Dawley rats, aged 21 days, were used. These were divided equally into one of three groups, control (CG), sham (SG) or EMF (EMFG). CG was not exposed to any procedure. SG rats were kept inside a cage, without being exposed to the effect of EMF, for 1 h a day on postnatal days 22-59, inclusive. EMFG rats were exposed to continuous 900-MHz EMF for 1 h a day under the same conditions as those for the SG rats. Rats were sacrificed on postnatal day 60, and the kidney and bladder tissues were removed. Tissues were stained with hematoxylin and eosin (H&E) and Masson trichrome for histomorphological evaluation. The TUNEL method was used to assess apoptosis. Transmission electron microscopy (TEM) was also used for the kidney tissue. Oxidant/antioxidant parameters were studied in terms of biochemical values.

RESULTS: The findings showed that tissue malondialdehyde increased in EMFG compared to CG and SG in both kidney ($p = 0.004$ and $p = 0.004$, respectively) and bladder tissue ($p = 0.004$, $p = 0.006$, respectively), while catalase and glutathione levels decreased compared to CG ($p = 0.004$; $p = 0.004$, respectively) and SG ($p = 0.004$; $p = 0.004$, respectively). In the EMF group, pathologies such as dilatation and vacuolization in the distal and proximal tubules, degeneration in glomeruli and an increase in cells tending to apoptosis were observed in kidney tissue. In bladder tissue, degeneration in the transitional epithelium and stromal irregularity and an increase in cells tending to apoptosis were observed in EMFG. Additionally, EMFG samples exhibited glomerular capillary degeneration with capillary basement membranes under TEM.

CONCLUSIONS: We conclude that continuous exposure to the effect of 900-MHz EMF for 1 h a day on postnatal days 22-59, inclusive, causes an increase in oxidative stress and various pathological changes in male rat kidney and bladder tissues.

<https://www.ncbi.nlm.nih.gov/pubmed/28747141>

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Effects of folic acid on rat kidney exposed to 900 MHz EMR

Deniz OG, Kıvrak EG, Kaplan AA, Altunkaynak BZ. Effects of folic acid on rat kidney exposed to 900 MHz electromagnetic radiation. *J Microsc Ultrastruct.* 2017 Oct-Dec;5(4):198-205. doi: 10.1016/j.jmau.2017.06.001

Highlights

- The kidneys of adult male rats were investigated after exposure to 900-MHz electromagnetic radiation.
- Folic acid exhibited protective effects in the kidney against the side-effects of electromagnetic radiation exposure.
- Changes in volume and numbers of glomeruli in the kidney were analyzed using unbiased stereological methods.

Abstract

Because of increased use of cell phones, the purpose of this study was to investigate the oxidative damage caused by electromagnetic radiation (EMR) emitted by cell phones and histological and morphometrical determination of the possible protective role of folic acid (FA) in preventing the detrimental effects of EMR on the kidney. Twenty-four adult male Wistar albino rats were divided into control (Cont), EMR, EMR + FA and FA groups, each containing six rats. The EMR and EMR + FA groups were exposed to EMR for 60 min a day over a period of 21 days, while no EMR exposure was applied to the Cont and FA groups. The source of the EMR was an EMR device which emits a digital signal producing 900-MHz frequency radiation. The generator connected to a one-monopole antenna was used in this study and the rats were placed in the plexiglass restrainer at an equal distance from the monopole antenna. Following the experimental period, and after tissue processing, a physical disector-Cavalieri method combination was applied to the sections. The mean volume of the cortex, medulla, proximal and distal tubules increased significantly in the EMR groups compared to the Cont group ($p < 0.01$). Contrarily, the total number of glomeruli in the EMR group decreased compared to the Cont group ($p < 0.01$). The protective effects of FA was observed in the kidney ($p < 0.05$).

In conclusion, the 900-MHz EMR leads to kidney damage. FA may exhibit a protective effect against the adverse effects of EMR exposure in terms of the total number of glomeruli.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6025785/>

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Effect of 900 MHz GSM Mobile Phone RF Radiation on Estrogen Receptor Methylation Status in Colon Cells

Mokarram P, Sheikhi M, Mortazavi SMJ, Saeb S, Shokrpour N. Effect of Exposure to 900 MHz GSM Mobile Phone Radiofrequency Radiation on Estrogen Receptor Methylation Status in Colon Cells of Male Sprague Dawley Rats. *J Biomed Phys Eng.* 2017 Mar 1;7(1):79-86..

Abstract

BACKGROUND: Over the past several years, the rapidly increasing use of mobile phones has raised global concerns about the biological effects of exposure to radiofrequency (RF) radiation. Numerous studies have shown that exposure to electromagnetic fields (EMFs) can be associated with effects on the nervous, endocrine, immune, cardiovascular, hematopoietic and ocular systems. In spite of genetic diversity, the onset and progression of cancer can be controlled by epigenetic mechanisms such as gene promoter methylation. There are extensive studies on the epigenetic changes of the tumor suppressor genes as well as the identification of methylation biomarkers in colorectal cancer. Some studies have revealed that genetic changes can be induced by exposure to RF radiation. However, whether or not RF radiation is capable of inducing epigenetic alteration has not been clarified yet. To date, no study has been conducted on the effect of radiation on epigenetic alterations in colorectal cancer (CRC). Several studies have also shown that methylation of estrogen receptor α (ER α), MYOD, MGMT, SFRP2 and P16 play an important role in CRC. It can be hypothesized that RF exposure can be a reason for the high incidence of CRC in Iran. This study aimed to investigate whether epigenetic pattern of ER α is susceptible to RF radiation and if RF radiation can induce radioadaptive response as epigenetic changes after receiving the challenge dose (γ -ray).

MATERIAL AND METHOD: 40 male Sprague-Dawley rats were divided into 4 equal groups

(Group I: exposure to RF radiation of a GSM cell phone for 4 hours and sacrificed after 24 hours; Group II: RF exposure for 4 hours, exposure to Co-60 gamma radiation (3 Gy) after 24 hours and sacrificed after 72 hrs; Group III: only 3Gy gamma radiation; Group 4: control group). DNA from colon tissues was extracted to evaluate the methylation status by methylation specific PCR.

RESULTS: Our finding showed that exposure to GSM cell phone RF radiation was capable of altering the pattern of ER α gene methylation compared to that of non-exposed controls. Furthermore, no adaptive response phenomenon was induced in the pattern of ER α gene methylation after exposure to the challenging dose of Co-60 γ -rays.

CONCLUSION: It can be concluded that exposure to RF radiation emitted by GSM mobile phones can lead to epigenetic detrimental changes in ER α promoter methylation pattern.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5401136/>

4.3. Effects on memory and brain functioning

Effects of 1.8 GHz Radiofrequency Fields on the Emotional Behavior and Spatial Memory of Adolescent Mice

Zhang JP, Zhang KY, Guo L, Chen QL, Gao P, Wang T, Li J, Guo GZ, Ding GR. Effects of 1.8 GHz Radiofrequency fields on the emotional behavior and spatial memory of adolescent mice. *Int J Environ Res Public Health*. 2017 Nov 5;14(11). pii: E1344. doi: 10.3390/ijerph14111344.

Abstract

The increasing use of mobile phones by teenagers has raised concern about the cognitive effects of radiofrequency (RF) fields. In this study, we investigated the effects of 4-week exposure to a 1.8 GHz RF field on the emotional behavior and spatial memory of adolescent male mice. Anxiety-like behavior was evaluated by open field test (OFT) and elevated plus maze (EPM) test, while depression-like behavior was evaluated by sucrose preference test (SPT), tail suspension test (TST) and forced swim test (FST). The spatial learning and memory ability were evaluated by Morris water maze (MWM) experiments. The levels of amino acid neurotransmitters were determined by liquid chromatography-mass spectrometry (LC-MS). The histology of the brain was examined by hematoxylin-eosin (HE) staining. It was found that the depression-like behavior, spatial memory ability and histology of the brain did not change obviously after RF exposure. However, the anxiety-like behavior increased in mice, while, the levels of γ -aminobutyric acid (GABA) and aspartic acid (Asp) in cortex and hippocampus significantly decreased after RF exposure. These data suggested that RF exposure under these conditions do not affect the depression-like behavior, spatial memory and brain histology in adolescent male mice, but it may however increase the level of anxiety, and GABA and Asp were probably involved in this effect.

Open Access Paper: <http://www.mdpi.com/1660-4601/14/11/1344>

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Exposure to 835 MHz RF EMF induces autophagy in hippocampus but not in brain stem of mice

Kim JH, Yu DH, Kim HJ, Huh YH, Cho SW, Lee JK, Kim HG, Kim HR. Exposure to 835 MHz radiofrequency electromagnetic field induces autophagy in hippocampus but not in brain stem of mice. *Toxicol Ind Health*. 2017 Jan 1:748233717740066. doi: 10.1177/0748233717740066.

Abstract

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

<https://www.ncbi.nlm.nih.gov/pubmed/29166827>

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Effect of Ginkgo biloba on hippocampus of rats exposed to long-term cellphone radiation

Gevrek, F. Histopathological, immunohistochemical, and stereological analysis of the effect of Ginkgo biloba (Egb761) on the hippocampus of rats exposed to long-term cellphone radiation. *Histology and Histopathology*. 33(5):463-473. May 2018. DOI: 10.14670/HH-11-943

Abstract

Cellular phones are major sources of electromagnetic radiation (EMR) that can penetrate the human body and pose serious health hazards. The increasingly widespread use of mobile communication systems has raised concerns about the effects of cellphone radiofrequency (RF) on the hippocampus because of its close proximity to radiation during cellphone use. The effects of cellphone EMR exposure on the hippocampus of rats and the possible counteractive effects of Ginkgo biloba (Egb761) were aimed to investigate. Rats were divided into three groups: Control, EMR, and EMR+Egb761. The EMR and EMR+Egb761 groups were exposed to cellphone EMR for one month. Egb761 was also administered to the EMR+Egb761 group.

Specifically, we evaluated the effect of RF exposure on rat hippocampi at harmful EMR levels (0.96 W/kg specific absorption rate [SAR]) for one month and also investigated the possible impact of Egb761 using stereological, TUNEL-staining, and immunohistochemical methods. An increase in apoptotic proteins (Bax, Acas-3) and a decrease in anti-apoptotic protein (Bcl-2) immuno-reactivity along with a decrease in the total granule and pyramidal cell count were noted in the EMR group. A decrease in Bax and Acas-3 and an increase in Bcl-2 immunoreactivity were observed in rats treated with Egb761 in addition to a decrease in TUNEL-stained apoptotic cells and a higher total viable cell number. In conclusion, chronic cellphone EMR exposure may affect hippocampal cell viability, and Egb761 may be used to mitigate some of the deleterious effects.

<https://www.ncbi.nlm.nih.gov/pubmed/29120031>

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Exposure to GSM 900-MHz mobile radiation impaired inhibitory avoidance memory consolidation in rat: Involvements of opioidergic and nitrenergic systems

Ahmadi S, Alavi SS, Jadidi M, Ardjmand A. Exposure to GSM 900-MHz mobile radiation impaired inhibitory avoidance memory consolidation in rat: Involvements of opioidergic and nitrenergic systems. *Brain Research*. 1701:36-45. Dec 2018.

<https://doi.org/10.1016/j.brainres.2018.07.016>.

Highlights

- Four weeks of exposure to GSM radiation impaired IA memory performance.
- Post-training i.c.v. injections of naloxone recovered the impairment of IA memory.
- Pre-test i.c.v. injections of L-NAME impaired the positive effect of naloxone
- Pre-test co-administration of L-arginine and L-NAME recovered the impairment.
- Opioid and NO systems are involved in the effects of GSM exposure on IA memory.

Abstract

The use of mobile phones is increasing, and the main health concern is the possible deleterious effects of radiation on brain functioning. The present study aimed to examine the effects of exposure to a global system for mobile communication (GSM) with mobile phones on inhibitory avoidance (IA) memory performance as well as the involvement of endogenous opioids and nitric oxide (NO) in this task. Male Wistar rats, 10–12 weeks old, were used. The results showed that four weeks of mobile phone exposure impaired IA memory performance in rats. The results also revealed that post-training, but not pre-training, as well as pre-test intracerebroventricular (i.c.v.) injections of naloxone (0.4, 4 and 40 ng/rat), dose-dependently recovered the impairment of IA memory performance induced by GSM radiation. Additionally, the impairment of IA memory performance was completely recovered in the exposed animals with post-training treatment of naloxone (40 ng/rat) plus pre-test i.c.v. injections of L-arginine (100 and 200 nmol/rat). However, pre-test i.c.v. injections of L-NAME (10 and 20 nmol/rat), impaired IA memory performance in the animals receiving post-training naloxone (40 ng/rat). In the animals receiving post-training naloxone treatment, the impairment of IA memory performance due to pre-test i.c.v. injections of L-NAME was recovered by the pre-test co-administration of L-arginine. It was concluded that the recovery from impairment of IA memory in GSM-exposed

animals with post-training naloxone treatment was the result of blockade of the opioidergic system in early memory consolidation as well as activation of the nitrergic system in the retrieval phase of memory.

<https://www.sciencedirect.com/science/article/pii/S0006899318304001>

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Hippocampal alterations triggered by acute exposure of mice to GSM 1800 MHz mobile phone radiation

Fragopoulou AF, Polyzos A, Papadopoulou MD, Sansone A, Manta AK, Balafas E, Kostomitsopoulos N, Skouroliakou A, Chatgialiloglu C, Georgakilas A, Stravopodis DJ, Ferreri C, Thanos D, Margaritis LH. Hippocampal lipidome and transcriptome profile alterations triggered by acute exposure of mice to GSM 1800 MHz mobile phone radiation: An exploratory study. *Brain Behav.* 2018 Jun;8(6):e01001. doi: 10.1002/brb3.1001.

Abstract

BACKGROUND: The widespread use of wireless devices during the last decades is raising concerns about adverse health effects of the radiofrequency electromagnetic radiation (RF-EMR) emitted from these devices. Recent research is focusing on unraveling the underlying mechanisms of RF-EMR and potential cellular targets. The "omics" high-throughput approaches are powerful tools to investigate the global effects of RF-EMR on cellular physiology.

METHODS: In this work, C57BL/6 adult male mice were whole-body exposed (nExp = 8) for 2 hr to GSM 1800 MHz mobile phone radiation at an average electric field intensity range of 4.3-17.5 V/m or sham-exposed (nSE = 8), and the RF-EMR effects on the hippocampal lipidome and transcriptome profiles were assessed 6 hr later.

RESULTS: The data analysis of the phospholipid fatty acid residues revealed that the levels of four fatty acids [16:0, 16:1 (6c + 7c), 18:1 9c, eicosapentaenoic acid omega-3 (EPA, 20:5 ω3)] and the two fatty acid sums of saturated and monounsaturated fatty acids (SFA and MUFA) were significantly altered ($p < 0.05$) in the exposed group. The observed changes indicate a membrane remodeling response of the tissue phospholipids after nonionizing radiation exposure, reducing SFA and EPA, while increasing MUFA residues. The microarray data analysis demonstrated that the expression of 178 genes changed significantly ($p < 0.05$) between the two groups, revealing an impact on genes involved in critical biological processes, such as cell cycle, DNA replication and repair, cell death, cell signaling, nervous system development and function, immune system response, lipid metabolism, and carcinogenesis.

CONCLUSIONS: This study provides preliminary evidence that mobile phone radiation induces hippocampal lipidome and transcriptome changes that may explain the brain proteome changes and memory deficits previously shown by our group.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5991598/>

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Long-term exposure to continuous 900 MHz EMF disrupts cerebellar morphology in young adult male rats

Aslan A, İkinci A, Baş O, Sönmez OF, Kaya H, Odacı E. Long-term exposure to a continuous 900 MHz electromagnetic field disrupts cerebellar morphology in young adult male rats. *Biotech Histochem.* 2017 May 16:1-7. doi: 10.1080/10520295.2017.1310295.

Abstract

The pathological effects of exposure to an electromagnetic field (EMF) during childhood and adolescence may be greater than those from exposure during adulthood. We investigated possible pathological changes in the cerebellum of adolescent rats exposed to 900 MHz EMF daily for 25 days. We used three groups of six 21-day-old male rats as follows: unexposed control group (Non-EG), sham-exposed group (Sham-EG) and an EMF-exposed group (EMF-EG). EMF-EG rats were exposed to EMF in an EMF cage for 1 h daily from postnatal days 21 through 46. Sham-EG rats were placed in the EMF cage for 1 h daily, but were not subjected to EMF. No procedures were performed on the Non-EG rats. The cerebellums of all animals were removed on postnatal day 47, sectioned and stained with cresyl violet for histopathological and stereological analyses. We found significantly fewer Purkinje cells in the EMF-EG group than in the Non-EG and Sham-EG groups. Histopathological evaluation revealed alteration of normal Purkinje cell arrangement and pathological changes including intense staining of neuron cytoplasm in the EMF-EG group. We found that exposure to continuous 900 MHz EMF for 1 h/day during adolescence can disrupt cerebellar morphology and reduce the number of Purkinje cells in adolescent rats.

<https://www.ncbi.nlm.nih.gov/pubmed/28506085>

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835 MHz RF-EMF decreases expression of calcium channels, inhibits apoptosis, but induces autophagy in mouse hippocampus

Kim JH, Sohn UD, Kim HG, Kim HR. Exposure to 835 MHz RF-EMF decreases the expression of calcium channels, inhibits apoptosis, but induces autophagy in the mouse hippocampus. *Korean J Physiol Pharmacol.* 2018 May;22(3):277-289. doi: 10.4196/kjpp.2018.22.3.277.

Abstract

The exponential increase in the use of mobile communication has triggered public concerns about the potential adverse effects of radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phones on the central nervous system (CNS). In this study, we explored the relationship between calcium channels and apoptosis or autophagy in the hippocampus of C57BL/6 mice after RF-EMF exposure with a specific absorption rate (SAR) of 4.0 W/kg for 4

weeks. Firstly, the expression level of voltage-gated calcium channels (VGCCs), a key regulator of the entry of calcium ions into the cell, was confirmed by immunoblots. We investigated and confirmed that pan-calcium channel expression in hippocampal neurons were significantly decreased after exposure to RF-EMF. With the observed accumulation of autolysosomes in hippocampal neurons via TEM, the expressions of autophagy-related genes and proteins (e.g., LC3B-II) had significantly increased. However, down-regulation of the apoptotic pathway may contribute to the decrease in calcium channel expression, and thus lower levels of calcium in hippocampal neurons. These results suggested that exposure of RF-EMF could alter intracellular calcium homeostasis by decreasing calcium channel expression in the hippocampus; presumably by activating the autophagy pathway, while inhibiting apoptotic regulation as an adaptation process for 835 MHz RF-EMF exposure.

Open access paper: <http://pdf.medrang.co.kr/paper/pdf/Kjpp/Kjpp022-03-06.pdf>

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RF EMR exposure effects on amygdala morphology, place preference behavior and brain caspase-3 activity in rats

Narayanan, SN, Mohapatra, N, John, P, Suresh Kumar, NKR,. Nayak, SB, Gopalakrishna Bhat, P. Radiofrequency electromagnetic radiation exposure effects on amygdala morphology, place preference behavior and brain caspase-3 activity in rats. *Environ Toxicol Pharmacol.* 2018 Mar;58:220-229. doi: 10.1016/j.etap.2018.01.009.

Abstract

The purpose of the study was to evaluate the changes in amygdala morphology and emotional behaviors, upon exposure to chronic RF-EMR in adolescent rats. Four weeks old male albino Wistar rats were exposed to 900 MHz (power density: 146.60 $\mu\text{W}/\text{cm}^2$) from a mobile phone in silent-mode for 28 days. Amygdala morphology was studied using cresyl violet, TUNEL and Golgi-Cox staining. Place preference behavior was studied using light/dark chamber test and following this brain caspase-3 activity was determined. Number of healthy neurons was decreased in the basolateral amygdala and cortical amygdala but not in the central amygdala after RF-EMR exposure. It also induced apoptosis in the amygdala. RF-EMR exposure altered dendritic arborization pattern in basolateral amygdala but not in the central amygdala. Altered place preference and hyperactivity-like behavior was evident after RF-EMR exposure, but brain caspase-3 activity did not change. RF-EMR exposure perturbed normal cellular architecture of amygdala and this was associated with altered place preference.

<https://www.ncbi.nlm.nih.gov/pubmed/29413766>

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Effects of GSM and UMTS mobile telephony signals on neuron degeneration and blood-brain barrier permeation in the rat brain

Poullietier de Gannes F, Masuda H, Billaudel B, Poque-Haro E, Hurtier A, Lévêque P, Ruffié G, Taxile M, Veyret B, Lagroye I. Effects of GSM and UMTS mobile telephony signals on neuron degeneration and blood-brain barrier permeation in the rat brain. *Sci Rep.* 2017 Nov 14;7(1):15496. doi: 10.1038/s41598-017-15690-1.

Abstract

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

Excerpt

In the present work, BBB permeability in the whole rat brain increased significantly 50 days after repeated exposures: 3-fold for GSM and 2.4-fold for UMTS at 13 W/kg. A similar significant effect was seen in the whole brain with GSM-1800 at 0.26 W/kg. However, while the mean number of spots was quite similar at different BASAR levels, their distribution among the animals varied. For example, 20% of the 0.026 W/kg rats had between 4 and 5.5 spots, versus 45% of the 13 W/kg rats (data not shown). Thus, the effect was much stronger and consistent at 13 W/kg than at 0.026 W/kg or 0.26 W/kg. It is also noteworthy that the highest albumin levels were comparable to the highest background levels in cage-control rats (Fig. 3).

Open access paper: <https://www.nature.com/articles/s41598-017-15690-1>

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Effects of acute & chronic exposure to 900 MHz & 2100 MHz EMR on glutamate receptor signaling pathway

Gökçek-Saraç Ç, Er H, Kencebay Manas C, Kantar Gök D, Özen Ş, Derin N. Effects of acute and chronic exposure to both 900 MHz and 2100 MHz electromagnetic radiation on glutamate receptor signaling pathway. *Int J Radiat Biol.* 2017 Jun 1:1-29. doi: 10.1080/09553002.2017.1337279.

Abstract

PURPOSE: To demonstrate molecular effects of acute and chronic exposure to both 900 MHz and 2100 MHz radiofrequency electromagnetic radiation (RF-EMR) on the hippocampal level/activity of some of the enzymes - including PKA, CaMKII α , CREB, and p44/42 MAPK - from N-methyl-D-aspartate receptor (NMDAR) related signaling pathways.

MATERIALS AND METHODS: Rats were divided into following groups: Sham rats, rats exposed to 900 MHz and 2100 MHz RF-EMR for 2 h/day for acute (1 week) or chronic (10 weeks), respectively. The Western Blotting and activity measurement assays were used to assess the level/activity of the selected enzymes.

RESULTS: The obtained results have revealed that the hippocampal level/activity of selected enzymes was significantly higher in chronic groups as compared to acute groups at both 900 MHz and 2100 MHz RF-EMR exposure. In addition, hippocampal level/activity of selected enzymes was significantly higher at 2100 MHz RF-EMR than 900 MHz RF-EMR in both acute and chronic groups.

CONCLUSION: The present study provides experimental evidence that both exposure duration (1 week versus 10 weeks) and different carrier frequencies (900 MHz versus 2100 MHz) had different effects on protein expression of hippocampus in Wistar rats, which might encourage further research on protection against RF-EMR exposure.

<https://www.ncbi.nlm.nih.gov/pubmed/28565929>

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Effect of low level subchronic microwave radiation on rat brain

Deshmukh PS, Megha K, Nasare N, Banerjee BD, Ahmed RS, Abegaonkar MP, Tripathi AK, Mediratta PK. Effect of low level subchronic microwave radiation on rat brain. *Biomed Environ Sci.* 2016 Dec;29(12):858-867. doi: 10.3967/bes2016.115.

Abstract

OBJECTIVE: The present study was designed to investigate the effects of subchronic low level microwave radiation (MWR) on cognitive function, heat shock protein 70 (HSP70) level and DNA damage in brain of Fischer rats.

METHODS: Experiments were performed on male Fischer rats exposed to microwave radiation for 90 days at three different frequencies: 900, 1800, and 2450 MHz. Animals were divided into 4 groups: Group I: Sham exposed, Group II: animals exposed to microwave radiation at 900 MHz and specific absorption rate (SAR) 5.953×10^{-4} W/kg, Group III: animals exposed to 1800 MHz at SAR 5.835×10^{-4} W/kg and Group IV: animals exposed to 2450 MHz at SAR 6.672×10^{-4} W/kg. All the animals were tested for cognitive function using elevated plus maze and Morris water maze at the end of the exposure period and subsequently sacrificed to collect brain tissues. HSP70 levels were estimated by ELISA and DNA damage was assessed using alkaline comet assay.

RESULTS: Microwave exposure at 900-2450 MHz with SAR values as mentioned above lead to decline in cognitive function, increase in HSP70 level and DNA damage in brain.

CONCLUSION: The results of the present study suggest that low level microwave exposure at frequencies 900, 1800, and 2450 MHz may lead to hazardous effects on brain.

<https://www.ncbi.nlm.nih.gov/pubmed/28081746>

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Long-term exposure to 835 MHz RF-EMF induces hyperactivity, autophagy and demyelination in the cortical neurons of mice

Kim JH, Yu DH, Huh YH, Lee EH, Kim HG, Kim HR. Long-term exposure to 835 MHz RF-EMF induces hyperactivity, autophagy and demyelination in the cortical neurons of mice. *Sci Rep.* 2017 Jan 20;7:41129.

Abstract

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

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5247706/>

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Alterations of thymic morphology and antioxidant biomarkers in male rats following exposure to continuous 900 MHz EMF during adolescence

Kulaber A, Kerimoğlu G, Ersöz Ş, Çolakoğlu S, Odacı E. Alterations of thymic morphology and antioxidant biomarkers in 60-day-old male rats following exposure to a continuous 900 MHz electromagnetic field during adolescence. *Biotech Histochem.* 2017 Jun 9:1-7. doi: 10.1080/10520295.2017.1312525.

Abstract

We investigated changes in thymic tissue of male rats exposed to a 900 megahertz (MHz) electromagnetic field (EMF) on postnatal days 22-59. Three groups of six 21-day-old male Sprague-Dawley rats were allocated as: control (CG), sham (SG) and EMF (EMFG) groups. No procedure was performed on the CG rats. SG rats were placed in a Plexiglas cage for 1 h every day between postnatal days 22 and 59 without exposure to EMF. EMFG rats were placed in the same cage for the same periods as the SG rats and were exposed to 900 MHz EMF. Rats were sacrificed on postnatal day 60. Sections of thymus were stained for histological assessment. Oxidant/antioxidant parameters were investigated biochemically. Malondialdehyde (MDA) levels in EMFG increased compared to the other groups. Extravascular erythrocytes were observed in

the medullary/corticomedullary regions in EMFG sections. We found that 900 MHz EMF applied for 1 h/day on postnatal days 22-59 can increase tissue MDA and histopathological changes in male rat thymic tissue.

<https://www.ncbi.nlm.nih.gov/pubmed/28598680>

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Evaluation of oxidative injury in sciatic nerves of male rats exposed to continuous 900-MHz EMF throughout adolescence

Kerimoğlu G, Güney C, Ersöz Ş, Odacı E. A histopathological and biochemical evaluation of oxidative injury in the sciatic nerves of male rats exposed to a continuous 900-megahertz electromagnetic field throughout all periods of adolescence. *J Chem Neuroanat.* 2018 Jan 10. pii: S0891-0618(17)30212-0. doi: 10.1016/j.jchemneu.2018.01.001.

Abstract

The effects on human health of the electromagnetic field (EMF) emitted by mobile phones, used by approximately 7 billion people worldwide, have become an important subject for scientific research. Studies have suggested that the EMF emitted by mobile phones can cause oxidative stress in different tissues and age groups. Young people in adolescence, a time period when risky behaviors and dependences increase, use mobile phones more than adults. The EMF emitted by mobile phones, which are generally carried in the pocket or in bags when not in use, will very probably affect the sciatic nerve. No previous study has investigated the effect of mobile phone use in adolescence on peripheral nerve. This study was planned accordingly. Twenty-four male Sprague Dawley rats aged 21 days were divided equally into control (CGr), Sham (SGr) and EMF (EMFGr) groups. No procedure was performed on CGr rats. EMFGr were exposed to the effect of a 900-megahertz (MHz) EMF for 1 h at the same time every day between postnatal days 21-59 (the entire adolescent period) inside a cage in the EMF apparatus. SGr rats were placed inside the cage for 1 h every day without being exposed to EMF. All rats were sacrificed at the end of the study period, and 1 cm sections of sciatic nerve were extracted. Malondialdehyde (MDA), glutathione, catalase (CAT) superoxide dismutase (SOD) values were investigated biochemically in half of the right sciatic nerve tissues. The other halves of the nerve tissues were subjected to routine histopathological tissue procedures, sectioned and stained with hematoxylin and eosin (H&E) and Masson's trichrome. Histopathological evaluation of slides stained with Masson's trichrome and H&E revealed a normal appearance in Schwann cells and axons in all groups. However, there was marked thickening in the epineurium of sciatic nerves from EMFGr rats. MDA, SOD and CAT levels were higher in EMFGr than in CGr and SGr at biochemical analyses. Apoptotic index (AI) analysis revealed a significant increase in the number of TUNEL (+) cells when EMFGr was compared with CGr and SGr. In conclusion, our study results suggest that continuous exposure to a 900-MHz EMF for 1 h throughout adolescence can cause oxidative injury and thickening in the epineurium in the sciatic nerve in male rats.

<https://www.ncbi.nlm.nih.gov/pubmed/29331319>

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Histopathological, immunohistochemical, and stereological analysis of the effect of Gingko biloba (Egb761) on the hippocampus of rats exposed to long-term cellphone radiation

Gevrek F. Histopathological, immunohistochemical, and stereological analysis of the effect of Gingko biloba (Egb761) on the hippocampus of rats exposed to long-term cellphone radiation. *Histol Histopathol.* 2018 May;33(5):463-473. doi: 10.14670/HH-11-943.

Abstract

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

<https://www.ncbi.nlm.nih.gov/pubmed/29120031>

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Cell phone exposure induces apoptosis, mitochondrial oxidative stress & TRPV1 channel activation in hippocampus of rats

Ertilav K, Uslusoy F, Ataizi S, Nazıroğlu M. Long term exposure to cell phone frequencies (900 and 1800 MHz) induces apoptosis, mitochondrial oxidative stress and TRPV1 channel activation in the hippocampus and dorsal root ganglion of rats. *Metab Brain Dis.* 2018 Jan 13. doi: 10.1007/s11011-017-0180-4.

Abstract

Mobile phone providers use electromagnetic radiation (EMR) with frequencies ranging from 900 to 1800 MHz. The increasing use of mobile phones has been accompanied by several potentially pathological consequences, such as neurological diseases related to hippocampal (HIPPO) and dorsal root ganglion neuron (DRGN). The TRPV1 channel is activated different stimuli, including CapN, high temperature and oxidative stress. We investigated the contribution TRPV1 to mitochondrial oxidative stress and apoptosis in HIPPO and DRGN following long term exposure to 900 and 1800 MHz in a rat model. Twenty-four adult rats were equally divided into the following groups: (1) control, (2) 900 MHz, and (3) 1800 MHz exposure. Each experimental group was exposed to EMR for 60 min/ 5 days of the week during the one year. The 900 and 1800 MHz EMR exposure induced increases in TRPV1 currents, intracellular free calcium influx (Ca²⁺), reactive oxygen species (ROS) production, mitochondrial membrane depolarization (JC-1), apoptosis, and caspase 3 and 9 activities in the HIPPO and DRGN. These deleterious processes were further increased in the 1800 MHz experimental group compared to the 900 MHz exposure group. In conclusion, mitochondrial oxidative stress, programmed cell death and Ca²⁺ entry pathway through TRPV1 activation in the HIPPO and DRGN of rats were increased in the rat model following exposure to 900 and 1800 MHz cell frequencies. Our results suggest that exposure to 900 and 1800 MHz EMR may induce a dose-associated, TRPV1-mediated stress response.

<https://www.ncbi.nlm.nih.gov/pubmed/29332300>

4.4. Reproductive harm

Alteration of adaptive behaviors of progeny after maternal mobile phone exposure

Petitdant N, Lecomte A, Robidel F, Gamez, C, Blazy K, Villégier A-S. Alteration of adaptive behaviors of progeny after maternal mobile phone exposure. *Environ Sci Pollut Res Int.* 2018 Apr;25(11):10894-10903. doi: 10.1007/s11356-017-1178-5.

Abstract

Exposure of pregnant women to radiofrequency (RF) devices raises questions on their possible health consequences for their progeny. We examined the hazard threshold of gestational RF on the progeny's glial homeostasis, sensory-motor gating, emotionality, and novelty seeking and tested whether maternal immune activation would increase RF toxicity. Pregnant dams were daily restrained with loop antennas adjoining the abdomen (fetus body specific absorption rates (SAR): 0, 0.7, or 2.6 W/kg) and received three lipopolysaccharide (LPS) intra-peritoneal injections (0 or 80 µg/kg). Scores in the prepulse startle inhibition, fear conditioning, open field, and elevated plus maze were assessed at adolescence and adulthood. Glial fibrillary acidic protein (GFAP) and interleukines-1 beta (ILs) were quantified. LPS induced a SAR-dependent reduction of the prepulse startle inhibition in adults. Activity in the open field was reduced at 2.6 W/kg at adolescence. GFAP and ILs, emotional memory, and anxiety-related behaviors were not modified. These data support the hypothesis that maternal immune

activation increased the developmental RF exposure-induced long-term neurobiological impairments. These data support the fact that fetuses who receive combined environmental exposures with RF need special attention for protection.

<https://www.ncbi.nlm.nih.gov/pubmed/29397508>

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RF EMR from cell phone causes defective testicular function in male Wistar rats

Oyewopo AO, Olaniyi SK, Oyewopo CI, Jimoh AT. Radiofrequency electromagnetic radiation from cell phone causes defective testicular function in male Wistar rats. *Andrologia*. 2017 Dec;49(10). doi: 10.1111/and.12772.

Abstract

Cell phones have become an integral part of everyday life. As cell phone usage has become more widespread, concerns have increased regarding the harmful effects of radiofrequency electromagnetic radiation from these devices. The current study was undertaken to investigate the effects of the emitted radiation by cell phones on testicular histomorphometry and biochemical analyses. Adult male Wistar rats weighing 180-200 g were randomly allotted to control, group A (switched off mode exposure), group B (1-hr exposure), group C (2-hr exposure) and group D (3-hr exposure). The animals were exposed to radiofrequency electromagnetic radiation of cell phone for a period of 28 days. Histomorphometry, biochemical and histological investigations were carried out. The histomorphometric parameters showed no significant change ($p < .05$) in the levels of germinal epithelial diameter in all the experimental groups compared with the control group. There was no significant change ($p < .05$) in cross-sectional diameter of all the experimental groups compared with the control group. Group D rats showed a significant decrease ($p < .05$) in lumen diameter compared with group B rats. There was an uneven distribution of germinal epithelial cells in groups B, C and D. However, there was degeneration of the epithelia cells in group D when compared to the control and group B rats. Sera levels of malondialdehyde (MDA) and superoxide dismutase (SOD), which are markers of reactive oxygen species, significantly increased (MDA) and decreased (SOD), respectively, in all the experimental groups compared with the control group. Also sera levels of gonadotropic hormones (FSH, LH and testosterone) significantly decreased ($p < .05$) in groups C and D compared with the control group. The study demonstrates that chronic exposure to radiofrequency electromagnetic radiation of cell phone leads to defective testicular function that is associated with increased oxidative stress and decreased gonadotropic hormonal profile.

<https://www.ncbi.nlm.nih.gov/pubmed/28261838>

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Effect of 2G and 3G Cell Phone Radiation on Developing Liver of Chick Embryo - Comparative Study

D'Silva MH, Swer RT, Anbalagan J, Rajesh B. Effect of Radiofrequency Radiation Emitted from 2G and 3G Cell Phone on Developing Liver of Chick Embryo - A Comparative Study. J Clin Diagn Res. 2017 Jul;11(7):AC05-AC09. doi: 10.7860/JCDR/2017/26360.10275.

Abstract

INTRODUCTION: The increasing scientific evidence of various health hazards on exposure of Radiofrequency Radiation (RFR) emitted from both the cell phones and base stations have caused significant media attention and public discussion in recent years. The mechanism of interaction of RF fields with developing tissues of children and fetuses may be different from that of adults due to their smaller physical size and variation in tissue electromagnetic properties. The present study may provide an insight into the basic mechanisms by which RF fields interact with developing tissues in an embryo.

AIM: To evaluate the possible tissue and DNA damage in developing liver of chick embryo following chronic exposure to Ultra-High Frequency/Radiofrequency Radiation (UHF/RFR) emitted from 2G and 3G cell phone.

MATERIALS AND METHODS: Fertilized chick embryos were incubated in four groups. Group A-experimental group exposed to 2G radiation (60 eggs), Group B- experimental group exposed to 3G radiation (60 eggs), Group C- sham exposed control group (60 eggs) and Group D- control group (48 eggs). On completion of scheduled duration, the embryos were collected and processed for routine histological studies to check structural changes in liver. The nuclear diameter and karyorrhexis changes of hepatocytes were analysed using oculometer and square reticule respectively. The liver procured from one batch of eggs from all the four groups was subjected to alkaline comet assay technique to assess DNA damage. The results were compared using one-way ANOVA test.

RESULTS: In our study, the exposure of developing chick embryos to 2G and 3G cell phone radiations caused structural changes in liver in the form of dilated sinusoidal spaces with haemorrhage, increased vacuolations in cytoplasm, increased nuclear diameter and karyorrhexis and significantly increased DNA damage.

CONCLUSION: The chronic exposure of chick embryo liver to RFR emitted from 2G and 3G cell phone resulted in various structural changes and DNA damage. The changes were more pronounced in 3G experimental group. Based on these findings it is necessary to create awareness among public about the possible ill effects of RFR exposure from cell phone.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5583901/>

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Mobile phone (1800MHz) radiation impairs female reproduction in mice through stress induced inhibition of ovarian & uterine activity

Shahin S, Singh SP, Chaturvedi CM. Mobile Phone (1800MHz) Radiation Impairs Female Reproduction in Mice, *Mus musculus*, through Stress Induced Inhibition of Ovarian and Uterine Activity. *Reprod Toxicol*. 2017 Aug 2. pii: S0890-6238(17)30167-3.

Highlights

- Mice exposed to mobile phone radiation (MPR) in different operative modes.
- Ovarian & uterine histopathology, steroidogenesis & stress parameters were checked.
- Degenerative changes & reduced follicle count were observed in MPR exposed ovary.
- MPR resulted significant decrease in ovarian steroidogenic proteins & sex steroids.
- MPR induced oxidative & nitrosative stress impairs reproductive functions in mice.

Abstract

Present study investigated the long-term effects of mobile phone (1800MHz) radiation in stand-by, dialing and receiving modes on the female reproductive function (ovarian and uterine histology, and steroidogenesis) and stress responses (oxidative and nitrosative stress). We observed that mobile phone radiation induces significant elevation in ROS, NO, lipid peroxidation, total carbonyl content and serum corticosterone coupled with significant decrease in antioxidant enzymes in hypothalamus, ovary and uterus of mice. Compared to control group, exposed mice exhibited reduced number of developing and mature follicles as well as corpus lutea. Significantly decreased serum levels of pituitary gonadotrophins (LH, FSH), sex steroids (E2 and P4) and expression of SF-1, StAR, P-450scc, 3 β -HSD, 17 β -HSD, cytochrome P-450 aromatase, ER- α and ER- β were observed in all the exposed groups of mice, compared to control. These findings suggest that mobile phone radiation induces oxidative and nitrosative stress, which affects the reproductive performance of female mice.

<https://www.ncbi.nlm.nih.gov/pubmed/28780396>

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Biological effects of cell-phone radiofrequency waves exposure on fertilization in mice; an in vivo and in vitro study

Fatehi D, Anjomshoa M, Mohammadi M, Seify M, Rostamzadeh A. Biological effects of cell-phone radiofrequency waves exposure on fertilization in mice; an in vivo and in vitro study. Middle East Fertility Society Journal, 23(2):148-153. June 2018.

Abstract

Increasing use of cell-phone is one of the most important risk factors for population health. We designed an experimental study aimed at evaluating the effects of cell-phone radiofrequency (RF) waves exposure on fertilization in mice. Two hundred male and female NMRI-mice were used. One hundred males divided in five groups (n = 20) as control and exposed groups. Those irradiated with cell-phone RF in "Standby-mode" 1, 5 and 10 h daily named groups II, III and IV; respectively. Group V irradiated with cell-phone on "Active-mode" one hour daily. After 30 days irradiation, 50 males and 50 females were kept 24 h to assess their embryos. Fifty males were sacrificed to evaluate both in vitro and in vivo parameters, and 50 females received PMSG & HCG for both quantitative and qualitative evaluation. Comparing groups III, IV and V with control-group showed significantly decreased in the number of two-cell embryos (p = .000); however, a significant increase was found in the number of dead embryos (p = .000). Furthermore, 5 h daily irradiation significantly decreased grade-A embryos (p = .015); while, it significantly increased grade-B, C and D embryos (p-values = 0.026, 0.007, 0.006; respectively). Moreover, comparing groups IV and V to control-group, significant increase was found in

pregnancy duration ($p = .005$, $p = .009$; respectively). However, in the mentioned groups a significant decrease was seen in number of newborn mice ($p = .001$, $p = .004$; respectively). In conclusion our findings showed that the cell-phone radiation can affect development of embryos as well as the number of newborn and pregnancy duration in NMRI-mouse, which might be a significant cause of reproductive failure.

Open access paper: <https://www.sciencedirect.com/science/article/pii/S1110569017301875>

The applied frequency of the waves was 900 MHz irradiated from a Nokia cell-phone (Nokia 1100, Finland). In case of irradiation, the distance between cell-phone and mouse was 10 cm.

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Effect of electromagnetic waves from mobile phones on spermatogenesis in the era of 4G-LTE

Oh JJ, Byun S, Lee SE, Choe G, Hong SK. Effect of electromagnetic waves from mobile phones on spermatogenesis in the era of 4G-LTE. *Biomed Res Int.* 2018 Jan 29;2018:1801798. doi: 10.1155/2018/1801798.

Abstract

Objective. To investigate the effect of long duration exposure to electromagnetic field from mobile phones on spermatogenesis in rats using 4G-LTE.

Methods. Twenty Sprague-Dawley male rats were placed into 4 groups according to the intensity and exposure duration: Group 1 (sham procedure), Group 2 (3 cm distance + 6 h exposure daily), Group 3 (10 cm distance + 18 h exposure daily), and Group 4 (3 cm distance + 18 h exposure daily). After 1 month, we compared sperm parameters and histopathological findings of the testis.

Results. The mean spermatid count ($\times 10^6/\text{ml}$) was 398.6 in Group 1, 365.40 in Group 2, 354.60 in Group 3, and 298.60 in Group 4 ($p = 0.041$). In the second review, the mean count of spermatogonia in Group 4 (43.00) was significantly lower than in Group 1 (57.00) and Group 2 (53.40) ($p < 0.001$ and $p = 0.010$, resp.). The sum of the germ cell counts was decreased in Group 4 compared to Groups 1, 2, and 3 ($p = 0.032$). The mean Leydig cell count was significantly decreased in Group 4 ($p < 0.001$).

Conclusions. The longer exposure duration of electromagnetic field decreased the spermatogenesis. Our findings warrant further investigations on the potential effects of EMF from mobile phones on male fertility.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896334/>

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1800 MHz mobile phone radiation induced oxidative and nitrosative stress leads to p53 dependent Bax mediated testicular apoptosis in mice

Shahin S, Singh SP, Chaturvedi CM. 1800 MHz mobile phone irradiation induced oxidative and nitrosative stress leads to p53 dependent Bax mediated testicular apoptosis in mice, *Mus musculus*. *J Cell Physiol*. 2018 Apr 10. doi: 10.1002/jcp.26558.

Abstract

Present study was carried out to investigate the effect of long-term mobile phone radiation exposure in different operative modes (Dialing, Receiving, and Stand-by) on immature male mice. Three-week old male mice were exposed to mobile phone (1800 MHz) radiation for 3 hr/day for 120 days in different operative modes. To check the changes/alteration in testicular histoarchitecture and serum testosterone level, HE staining and ELISA was performed respectively. Further, we have checked the redox status (ROS, NO, MDA level, and antioxidant enzymes: SOD, CAT, and GPx) by biochemical estimation, alteration in the expression of pro-apoptotic proteins (p53 and Bax), active executioner caspase-3, full length/uncleaved PARP-1 (DNA repair enzyme), anti-apoptotic proteins (Bcl-2 and Bcl-xL) in testes by immunofluorescence and cytosolic cytochrome-c by Western blot. Decreased seminiferous tubule diameter, sperm count, and viability along with increased germ cells apoptosis and decreased serum testosterone level, was observed in the testes of all the mobile phone exposed mice compared with control. We also observed that, mobile phone radiation exposure in all the three different operative modes alters the testicular redox status via increasing ROS, NO, and MDA level, and decreasing antioxidant enzymes levels leading to enhanced apoptosis of testicular cells by increasing the expression of pro-apoptotic and apoptotic proteins along with decreasing the expression of anti-apoptotic protein. On the basis of results, it is concluded that long-term mobile phone radiation exposure induced oxidative stress leads to apoptosis of testicular cells and thus impairs testicular function.

<https://www.ncbi.nlm.nih.gov/pubmed/29637556>

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Quantitative changes in testicular structure and function in rat exposed to mobile phone radiation

Çetkin M, Kızıllan N, Demirel C, Bozdağ Z, Erkıılıç S, Erbağcı H. Quantitative changes in testicular structure and function in rat exposed to mobile phone radiation. *Andrologia*. 2017 Dec;49(10). doi: 10.1111/and.12761.

Abstract

The possible effects of the electromagnetic fields (EMF) generated by mobile phones on reproductive functions have been discussed in recent years. The aim of this study was to evaluate the effects of EMF emitted from mobile phones on the rat testis morphology and

histopathology using stereological techniques. We also investigated cortisol, testosterone, FSH and LH levels. A total of thirty-two (n = 32) male Wistar albino rats were used in this study. Animals were randomly divided into four groups as control (C, n = 8), sham (Sh, n = 8), mobile phone speech (Sp, n = 8) and mobile phone standby (ST by). Morphometric measurements were made with the help of a computer-assisted stereological analysis system. The testis weight and volume were significantly lower in the EMF exposed groups. The mean volume fraction of interstitial tissue was higher, but the volume fraction of tubular tissue was lower in the EMF-exposed groups. The mean tubular and germinal tissue volume, seminiferous tubule diameter and germinal epithelium height were also lower in EMF exposed groups. The cortisol levels in the EMF-exposed groups were significantly higher. In conclusion, the EMF created by mobile phones caused morphologic and histological changes by the affecting germinal epithelium tissue negatively.

<https://www.ncbi.nlm.nih.gov/pubmed/28124386>

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Mobile-phone Radiation-induced Perturbation of Gene-expression Profiling, Redox Equilibrium & Sporadic-apoptosis Control in the Ovary of *Drosophila melanogaster*

Manta AK, Papadopoulou D, Polyzos AP, Fragopoulou AF, Skouropoulou AS, Thanos D, Stravopodis DJ, Margaritis LH. Mobile-phone Radiation-induced Perturbation of Gene-expression Profiling, Redox Equilibrium and Sporadic-apoptosis Control in the Ovary of *Drosophila melanogaster*. *Fly (Austin)*. 2017 Apr 3;11(2):75-95. doi: 10.1080/19336934.2016.1270487.

Abstract

BACKGROUND: The daily use by people of wireless communication devices has increased exponentially in the last decade, begetting concerns regarding its potential health hazards.

METHODS: *Drosophila melanogaster* four days-old adult female flies were exposed for 30 min to radiation emitted by a commercial mobile phone at a SAR of 0.15 W/kg and a SAE of 270 J/kg. ROS levels and apoptotic follicles were assayed in parallel with a genome-wide microarrays analysis.

RESULTS: ROS cellular contents were found to increase by 1.6 fold (x), immediately after the end of exposure, in follicles of pre-choriogenic stages (germarium - stage 10), while sporadically generated apoptotic follicles (germarium 2b and stages 7-9) presented with an averaged 2x upregulation in their sub-population mass, 4 h after fly's irradiation with mobile device. Microarray analysis revealed 168 genes being differentially expressed, 2 h post-exposure, in response to radiofrequency (RF) electromagnetic field-radiation exposure ($\geq 1.25x$, $P < 0.05$) and associated with multiple and critical biological processes, such as basic metabolism and cellular subroutines related to stress response and apoptotic death.

CONCLUSION: Exposure of adult flies to mobile-phone radiation for 30 min has an immediate impact on ROS production in animal's ovary, which seems to cause a global, systemic and non-targeted transcriptional reprogramming of gene expression, 2 h post-exposure, being finally followed by induction of apoptosis 4 h after the end of exposure. Conclusively, this unique type of pulsed radiation, mainly being derived from daily used mobile phones, seems capable of mobilizing critical cytopathic mechanisms, and altering fundamental genetic programs and networks in *D. melanogaster*.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5406167/>

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Effects of Simulated Mobile Phone EMR on Fertilization and Embryo Development

Chen H, Qu Z, Liu W. Effects of Simulated Mobile Phone Electromagnetic Radiation on Fertilization and Embryo Development. *Fetal Pediatr Pathol.* 2017 Apr;36(2):123-129. doi: 10.1080/15513815.2016.1261974.

Abstract

This study investigated the effects of 935-MHz electromagnetic radiation (ER) on fertilization and subsequent embryonic development in mice. Ovulating mice were irradiated at three ER intensities for 4 h/day (d) or 2 h/d for three consecutive days; the ova were then harvested for in vitro fertilization to observe the 6-h fertilization rate (6-FR), 72-h morula rate (72-MR), and 110-h blastula rate (110-BR). Compared with the control group, the 6-FR, 72-MR, and 110-BR were decreased in the low ER intensity group, but the differences were not significant; in the mid- and high-intensity ER groups, 72-MR and 110-BR in the 4 h/d and 2 h/d subgroups were decreased, showing significant differences compared with the control group. Moreover, the comparison between 4 h/d and 2 h/d subgroups showed significant differences. Mid- and high-intensity ER at 935 MHz can reduce the fertilization rate in mice, and reduce the blastulation rate, thus reducing the possibility of embryo implantation.

<https://www.ncbi.nlm.nih.gov/pubmed/27983879>

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RF radiation (900 MHz)-induced DNA damage and cell cycle arrest in testicular germ cells in mice

Pandey N, Giri S, Das S, Upadhaya P. Radiofrequency radiation (900 MHz)-induced DNA damage and cell cycle arrest in testicular germ cells in swiss albino mice. *Toxicol Ind Health.* 2017 Apr;33(4):373-384. doi: 10.1177/0748233716671206.

Abstract

Even though there are contradictory reports regarding the cellular and molecular changes

induced by mobile phone emitted radiofrequency radiation (RFR), the possibility of any biological effect cannot be ruled out. In view of a widespread and extensive use of mobile phones, this study evaluates alterations in male germ cell transformation kinetics following RFR exposure and after recovery. Swiss albino mice were exposed to RFR (900 MHz) for 4 h and 8 h duration per day for 35 days. One group of animals was terminated after the exposure period, while others were kept for an additional 35 days post-exposure. RFR exposure caused depolarization of mitochondrial membranes resulting in destabilized cellular redox homeostasis. Statistically significant increases in the damage index in germ cells and sperm head defects were noted in RFR-exposed animals. Flow cytometric estimation of germ cell subtypes in mice testis revealed 2.5-fold increases in spermatogonial populations with significant decreases in spermatids. Almost fourfold reduction in spermatogonia to spermatid turnover (1C:2C) and three times reduction in primary spermatocyte to spermatid turnover (1C:4C) was found indicating arrest in the premeiotic stage of spermatogenesis, which resulted in loss of post-meiotic germ cells apparent from testis histology and low sperm count in RFR-exposed animals. Histological alterations such as sloughing of immature germ cells into the seminiferous tubule lumen, epithelium depletion and maturation arrest were also observed. However, all these changes showed recovery to varied degrees following the post-exposure period indicating that the adverse effects of RFR on mice germ cells are detrimental but reversible. To conclude, RFR exposure-induced oxidative stress causes DNA damage in germ cells, which alters cell cycle progression leading to low sperm count in mice.

<https://www.ncbi.nlm.nih.gov/pubmed/27738269>

4.5. Other effects

Effects of 1.8 GHz radiofrequency field on microstructure and bone metabolism of femur in mice

Guo L, Zhang JP, Zhang KY, Wang HB, Wang H, An GZ, Zhou Y, Meng GL, Ding DR. Effects of 1.8 GHz radiofrequency field on microstructure and bone metabolism of femur in mice. *Bioelectromagnetics*. 2018 Jul;39(5):386-393. doi: 10.1002/bem.22125.

Abstract

To investigate the effects of 1.8 GHz radiofrequency (RF) field on bone microstructure and metabolism of femur in mice, C57BL/6 mice (male, age 4 weeks) were whole-body exposed or sham exposed to 1.8 GHz RF field. Specific absorption rates of whole body and bone were approximately 2.70 and 1.14 W/kg (6 h/day for 28 days). After exposure, microstructure and morphology of femur were observed by microcomputed tomography (micro-CT), Hematoxylin and Eosin (HE) and Masson staining. Subsequently, bone parameters were calculated directly from the reconstructed images, including structure model index, bone mineral density, trabecular bone volume/total volume, connectivity density, trabecular number, trabecular thickness, and trabecular separation. Biomarkers that reflect bone metabolism, such as serum

total alkaline phosphatase (ALP), bone-specific alkaline phosphatase (BALP), and tartrate-resistant acid phosphatase 5b (TRACP-5b), were determined by biochemical assay methods. Micro-CT and histology results showed that there was no significant change in bone microstructure and the above parameters in RF group, compared with sham group. The activity of serum ALP and BALP increased 29.47% and 16.82%, respectively, in RF group, compared with sham group ($P < 0.05$). In addition, there were no significant differences in the activity of serum TRACP-5b between RF group and sham group. In brief, under present experimental conditions, we did not find support for an effect of 1.8 GHz RF field on bone microstructure; however, it might promote metabolic function of osteoblasts in mice.

<https://www.ncbi.nlm.nih.gov/pubmed/29709060>

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GSM 900 MHz Microwave Radiation-Induced Alterations of Insulin Level and Histopathological Changes of Liver and Pancreas in Rat

Mortazavi SMJ, Owji SM, Shojaie-fard MB, Ghader-Panah M, Mortazavi SAR, Tavakoli-Golpayegani A, Haghani M, Taeb S, Shokrpour N, Koohi O. GSM 900 MHz Microwave Radiation-Induced Alterations of Insulin Level and Histopathological Changes of Liver and Pancreas in Rat. J Biomed Phys Eng. 2016 Dec 1;6(4):235-242.

Abstract

Background: The rapidly increasing use of mobile phones has led to public concerns about possible health effects of these popular communication devices. This study is an attempt to investigate the effects of radiofrequency (RF) radiation produced by GSM mobile phones on the insulin release in rats.

Methods: Forty two female adult Sprague Dawley rats were randomly divided into 4 groups. Group 1 were exposed to RF radiation 6 hours per day for 7 days. Group 2 received sham exposure (6 hours per day for 7 days). Groups 3 and 4 received RF radiation 3 hours per day for 7 days and sham exposure (3 hours per day), respectively. The specific absorption rate (SAR) of RF was 2.0 W/kg.

Results: Our results showed that RF radiations emitted from mobile phone could not alter insulin release in rats. However, mild to severe inflammatory changes in the portal spaces of the liver of rats as well as damage in the cells of islet of Langerhans were observed. These changes were linked with the duration of the exposures.

Conclusion: RF exposure can induce inflammatory changes in the liver as well causing damage in the cells of islet of Langerhans.

Open access paper: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5219574/>

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Effect of electromagnetic waves from mobile phone on immune status of male rats: possible protective role of vitamin D

El-Gohary O, Said MA. Effect of electromagnetic waves from mobile phone on immune status of male rats: possible protective role of vitamin D. *Can J Physiol Pharmacol.* 2017 Feb;95(2):151-156. doi: 10.1139/cjpp-2016-0218.

Abstract

There are considerable public concerns about the relationship between mobile phone radiation and human health. The present study assesses the effect of electromagnetic field (EMF) emitted from a mobile phone on the immune system in rats and the possible protective role of vitamin D. Rats were randomly divided into six groups: Group I: control group; Group II: received vitamin D (1000 IU/kg/day) orally; Group III: exposed to EMF 1 h/day; Group IV: exposed to EMF 2 h/day; Group V: exposed to EMF 1 h/day and received vitamin D (1000 IU/kg/day); Group VI: exposed to EMF 2 h/day and received vitamin D (1000 IU/kg/day). After 30 days of exposure time, 1 h/day EMF exposure resulted in significant decrease in immunoglobulin levels (IgA, IgE, IgM, and IgG); total leukocyte, lymphocyte, eosinophil and basophil counts; and a significant increase in neutrophil and monocyte counts. These changes were more increased in the group exposed to 2 h/day EMF. Vitamin D supplementation in EMF-exposed rats reversed these results when compared with EMF-exposed groups. In contrast, 7, 14, and 21 days of EMF exposure produced nonsignificant differences in these parameters among all experimental groups. We concluded that exposure to mobile phone radiation compromises the immune system of rats, and vitamin D appears to have a protective effect.

<https://www.ncbi.nlm.nih.gov/pubmed/27901344>

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Effects of long-term exposure to 900 MHz EMF on heart morphology and biochemistry of male adolescent rats

Kerimoğlu G, Mercantepe T, Erol HS, Turgut A, Kaya H, Çolakoğlu S, Odacı E. Effects of long-term exposure to 900 megahertz electromagnetic field on heart morphology and biochemistry of male adolescent rats. *Biotech Histochem.* 2016 Aug 11:1-10.

Abstract

The pathological effects of exposure to an electromagnetic field (EMF) during adolescence may be greater than those in adulthood. We investigated the effects of exposure to 900 MHz EMF during adolescence on male adult rats. Twenty-four 21-day-old male rats were divided into three equal groups: control (Cont-Gr), sham (Shm-Gr) and EMF-exposed (EMF-Gr). EMF-Gr rats were placed in an EMF exposure cage (Plexiglas cage) for 1 h/day between postnatal days 21 and 59 and exposed to 900 MHz EMF. Shm-Gr rats were placed inside the Plexiglas cage under the same conditions and for the same duration, but were not exposed to EMF. All animals

were sacrificed on postnatal day 60 and the hearts were extracted for microscopic and biochemical analyses. Biochemical analysis showed increased levels of malondialdehyde and superoxide dismutase, and reduced glutathione and catalase levels in EMF-Gr compared to Cont-Gr animals. Hematoxylin and eosin stained sections from EMF-Gr animals exhibited structural changes and capillary congestion in the myocardium. The percentage of apoptotic myocardial cells in EMF-Gr was higher than in either Shm-Gr or Cont-Gr animals. Transmission electron microscopy of myocardial cells of EMF-Gr animals showed altered structure of Z bands, decreased myofilaments and pronounced vacuolization. We found that exposure of male rats to 900 MHz EMF for 1 h/day during adolescence caused oxidative stress, which caused structural alteration of male adolescent rat heart tissue.

<https://www.ncbi.nlm.nih.gov/pubmed/27715326>

5.0. Animal Cell Sample (In Vitro) Studies

5.1. Oxidative stress, genotoxic effects and cancer

Exposure to radiation from single or combined radio frequencies provokes macrophage dysfunction in the RAW 264.7 cell line

López-Furelos A, Salas-Sánchez AA, Ares-Pena FJ, Leiro-Vidal JM, López-Martín E. Exposure to radiation from single or combined radio frequencies provokes macrophage dysfunction in the RAW 264.7 cell line. *Int J Radiat Biol.* 2018 Apr 30;1-12. doi: 10.1080/09553002.2018.1465610.

Abstract

PURPOSE: The aim of this study was to determine whether exposure to radiation from single or multiple radio-frequency (RF) signals at 900 and 2450 MHz would induce effects in the RAW 264.7 cell line.

MATERIALS AND METHODS: Cell cultures were exposed to single or combined RF for 4, 24, 48, or 72 h in a GTEM electromagnetic test chamber. At the end of the radiation exposure time, viability and cell growth were analyzed by flow cytometry, nitric oxide (NO) production was measured by colorimetry, the expression of HSP70 and TNF- α was ascertained by qPCR, and the phagocytic activity was observed by microscopy.

RESULTS: NO production increased after 48 h exposure at 2450 MHz, compared with controls. The group subjected to the combined interaction of two RFs showed an increase of HSP70 after 48 h exposure and a significant increase of NO and TNF- α after 72 h. The phagocytic activity of macrophages decreased in all groups as exposure time increased.

CONCLUSIONS: Our results indicated a decrease in phagocytic activity and an increase in inflammatory, cytoprotective, and cytotoxic responses in macrophages after continuous and combined exposure of multiple RF signals. Multiple RF interact in everyday life, the immune response in humans is unknown.

<https://www.ncbi.nlm.nih.gov/pubmed/29659305>

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In vitro non-thermal oxidative stress response after 1800 MHz radiofrequency radiation

Marjanovic Cermak AM, Pavicic I, Tariba Lovakovic B, Pizent A, Trosic I. In vitro non-thermal oxidative stress response after 1800 MHz radiofrequency radiation. *Gen Physiol Biophys.* 2017 Oct;36(4):407-414. doi: 10.4149/gpb_2017007.

Abstract

In this study possible connection between radiofrequency exposure (RF) and development of oxidative stress was investigated by measuring impairment in cellular oxidation-reduction

balance immediately after RF exposure. Fibroblast cells V79 were exposed for 10, 30 and 60 minutes to 1800 MHz RF radiation. Electric field strength was 30 V/m and specific absorption rate (SAR) was calculated to be 1.6 W/kg. Electromagnetic field was generated within Gigahertz Transversal Electromagnetic Mode cell (GTEM) equipped by signal generator, amplifier and modulator. Cell viability was determined by CCK-8 colorimetric assay and level of reactive oxygen species (ROS) was detected by dihydroethidium staining. Reduced glutathione (GSH) and glutathione peroxidase (GSH-Px) were used to assess cell antioxidant activity while lipid oxidative damage was evaluated measuring concentration of malondialdehyde. Viability of V79 cells remained within normal physiological values regardless of exposure time. Increased level of superoxide radicals was detected after 60-min exposure. Significantly higher GSH level was observed immediately after 10-min exposure with higher but insignificant activity of GSH-Px. Lipid oxidative damage in exposed cell samples was not observed. Short-term RF exposure revealed transient oxidation-reduction imbalance in fibroblast cells following adaptation to applied experimental conditions.

<https://www.ncbi.nlm.nih.gov/pubmed/28836500>

5.2. Effects on memory and brain functioning

Changes in numbers and size of synaptic vesicles of cortical neurons induced by exposure to 835 MHz RF EMF

Kim JH, Kim HJ, Yu DH, Kweon HS, Huh YH, Kim HR. Changes in numbers and size of synaptic vesicles of cortical neurons induced by exposure to 835 MHz radiofrequency-electromagnetic field. PLoS One. 2017 Oct 18;12(10):e0186416.

Abstract

We studied the effects of radiofrequency electromagnetic fields (RF-EMFs) exposure on neuronal functions of mice. Particularly, we focused on RF-EMF effects on synaptic vesicles (SVs), which store neurotransmitters at axon terminals or synaptic boutons. C57 BL/6 mice were exposed to 835 MHz RF-EMF (4.0 W/kg SAR, for 5 h daily) and alterations in SVs at presynaptic terminals in the cerebral cortex were determined. Ultrastructure of randomly selected cortical neurons was observed using typical electron microscopy and bio-high voltage electron microscopy (Bio-HVEM) methods, which enable the estimation of the numbers and size of SVs. The density of the SVs (number /10 μm^2 or 40 μm^3) was significantly decreased in the presynaptic boutons of cortical neurons after RF-EMF exposure. Furthermore, qPCR and immunoblotting analyses revealed that the expression of synapsins I/II (Syns I/II) genes and proteins were significantly decreased in the cortical neurons of RF-EMF exposed mice. The present study suggested that alteration of SVs and Syn levels may result in alterations of neurotransmitters in the cerebral cortex following RF-EMF exposure.

<https://www.ncbi.nlm.nih.gov/pubmed/29045446>

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Mitochondrial hyperpolarization and cytochrome-c release in microwave-exposed MCF-7 cells

Esmekaya MA, Canseven AG, Kayhan H, Tuysuz MZ, Sirav B, Seyhan N. Mitochondrial hyperpolarization and cytochrome-c release in microwave-exposed MCF-7 cells. *Gen Physiol Biophys*. 2016 Sep 12.

Abstract

This study examines the effects of a 2.1-GHz WCDMA-modulated microwave (MW) radiation on apoptotic activity and mitochondrial membrane potential ($\Delta\Psi_m$) in MCF-7 cells. The cells were exposed to the MW at a specific absorption rate (SAR) of 0.528 W/kg for 4 or 24 h. The antiproliferative effect of MW exposure was determined by the MTT test. Cytochrome-c and p53 levels were determined by an ELISA method. The relative $\Delta\Psi_m$ was analysed by JC-1 staining using flow cytometer. Apoptotic rate of the cells was measured by Annexin-V-FITC staining. All assays were performed after certain time of incubations (15 min-4 h) following MW exposure. MW-exposed cells showed a significant decrease in viability when compared to unexposed cells. A significantly larger decrease was observed after longer exposure. The percentage of apoptotic cells, amount of cytochrome-c, and relative $\Delta\Psi_m$ were significantly higher in MW-exposed cells. The percent of apoptotic cells and relative $\Delta\Psi_m$ in 24 h MW-exposed group was significantly higher than those in 4 h MW-exposed group. However, no significant change was observed in p53 levels. These results demonstrated that exposure to 2.1-GHz WCDMA-modulated MW radiation caused hyperpolarization of mitochondria that in turn induced apoptosis in MCF-7 cells.

<https://www.ncbi.nlm.nih.gov/pubmed/27615380>

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Activation of autophagy at cerebral cortex and apoptosis at brainstem are differential responses to 835 MHz RF-EMF exposure

Kim JH, Yu DH, Kim HR. Activation of autophagy at cerebral cortex and apoptosis at brainstem are differential responses to 835 MHz RF-EMF exposure. *Korean J Physiol Pharmacol*. 2017 Mar;21(2):179-188.

Abstract

With the explosive increase in exposure to radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phones, public concerns have grown over the last few decades with regard to the potential effects of EMF exposure on the nervous system in the brain. Many researchers have suggested that RF-EMFs can effect diverse neuronal alterations in the brain, thereby affecting neuronal functions as well as behavior. Previously, we showed that long-term exposure to 835 MHz RF-EMF induces autophagy in the mice brain. In this study, we explore whether short-term exposure to RF-EMF leads to the autophagy pathway in the cerebral cortex and brainstem at 835 MHz with a specific absorption rate (SAR) of 4.0 W/kg for 4 weeks. Increased levels of autophagy genes and proteins such as LC3B-II and Beclin1 were demonstrated and the accumulation of autophagosomes and autolysosomes was observed in cortical neurons whereas apoptosis pathways were up-regulated in the brainstem but not in the

cortex following 4 weeks of RF exposure. Taken together, the present study indicates that monthly exposure to RF-EMF induces autophagy in the cerebral cortex and suggests that autophagic degradation in cortical neurons against a stress of 835 MHz RF during 4 weeks could correspond to adaptation to the RF stress environment. However, activation of apoptosis rather than autophagy in the brainstem is suggesting the differential responses to the RF-EMF stresses in the brain system.

<https://www.ncbi.nlm.nih.gov/pubmed/28280411>

5.3. Reproductive harm

1950 MHz RF EMR Inhibits Testosterone Secretion of Mouse Leydig Cells

Lin YY, Wu T, Liu JY, Gao P, Li KC, Guo QY, Yuan M, Lang HY, Zeng LH, Guo GZ. 1950 MHz Radio Frequency Electromagnetic Radiation Inhibits Testosterone Secretion of Mouse Leydig Cells. *Int J Environ Res Public Health*. 2017 Dec 23;15(1). pii: E17. doi: 10.3390/ijerph15010017.

Abstract

More studies that are focused on the bioeffects of radio-frequency (RF) electromagnetic radiation that is generated from the communication devices, but there were few reports with confirmed results about the bioeffects of RF radiation on reproductive cells. To explore the effects of 1950 MHz RF electromagnetic radiation (EMR) on mouse Leydig (TM3) cells. TM3 cells were irradiated or sham-irradiated continuously for 24 h by the specific absorption rate (SAR) 3 W/kg radiation. At 0, 1, 2, 3, 4, and 5 days after irradiation, cell proliferation was detected by cell counting kit-8 (CCK-8) method, cell cycle distribution, percentage of apoptosis, and cellular reactive oxygen species (ROS) were examined by flow cytometry, Testosterone level was measured using enzyme-linked immunosorbent assay (ELISA) assay, messenger ribonucleic acid (mRNA) expression level of steroidogenic acute regulatory protein (StAR) and P450scc in TM3 cells was detected by real-time polymerase chain reaction (PCR). After being irradiated for 24 h, cell proliferation obviously decreased and cell cycle distribution, secretion capacity of Testosterone, and P450scc mRNA level were reduced. While cell apoptosis, ROS, and StAR mRNA level did not change significantly. The current results indicated that 24 h of exposure at 1950 MHz 3 W/kg radiation could cause some adverse effects on TM3 cells proliferation and Testosterone secretion, further studies about the biological effects in the reproductive system that are induced by RF radiation are also needed.

<https://www.ncbi.nlm.nih.gov/pubmed/29295490>

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Proteomic analysis of continuous 900-MHz RF EMF exposure in testicular tissue: a rat model of human cell phone exposure

Sephehrimanesh M, Kazemipour N, Saeb M, Nazifi S, Davis DL. Proteomic analysis of continuous 900-MHz radiofrequency electromagnetic field exposure in testicular tissue: a rat model of human cell phone exposure. *Environ Sci Pollut Res Int*. 2017 Apr 10. doi: 10.1007/s11356-017-8882-z.

Abstract

Although cell phones have been used worldwide, some adverse and toxic effects were reported for this communication technology apparatus. To analyze in vivo effects of exposure to radiofrequency-electromagnetic field (RF-EMF) on protein expression in rat testicular proteome, 20 Sprague-Dawley rats were exposed to 900 MHz RF-EMF for 0, 1, 2, or 4 h/day for 30 consecutive days. Protein content of rat testes was separated by high-resolution two-dimensional electrophoresis using immobilized pH gradient (pI 4-7, 7 cm) and 12% acrylamide and identified by MALDI-TOF/TOF-MS. Two protein spots were found differentially overexpressed ($P < 0.05$) in intensity and volume with induction factors 1.7 times greater after RF-EMF exposure. After 4 h of daily exposure for 30 consecutive days, ATP synthase beta subunit (ASBS) and hypoxia up-regulated protein 1 precursor (HYOU1) were found to be significantly up-regulated. These proteins affect signaling pathways in rat testes and spermatogenesis and play a critical role in protein folding and secretion in the endoplasmic reticulum. Our results indicate that exposure to RF-EMF produces increases in testicular proteins in adults that are related to carcinogenic risk and reproductive damage. In light of the widespread practice of men carrying phones in their pockets near their gonads, where exposures can exceed as-tested guidelines, further study of these effects should be a high priority.

<https://www.ncbi.nlm.nih.gov/pubmed/28397118>

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Exposure to mobile phone (900-1800 MHz) during pregnancy: tissue oxidative stress after childbirth

Bahreyni Toossi MH, Sadeghnia HR, Mohammad Mahdizadeh Feyzabadi M, Hosseini M, Hedayati M, Mosallanejad R, Beheshti F, Alizadeh Rahvar Z. Exposure to mobile phone (900-1800 MHz) during pregnancy: tissue oxidative stress after childbirth. *J Matern Fetal Neonatal Med.* 2017 Apr 23:1-6.

Abstract

BACKGROUND: The present study has investigated the effects of mobile phone (900-1800 MHz)-induced electromagnetic radiation on redox status in the heart, liver, kidney, cerebellum, and hippocampus of dams and the offspring mice.

MATERIALS AND METHODS: Pregnant Balb/C were divided into two groups including the control and the experimental group. The experimental group was exposed to mobile phone (900-1800 MHz), during pregnancy (2 h/d for 20 d). The dams and the offspring of both groups were sacrificed and tissues of interest were harvested immediately after delivery. Malondialdehyde (MDA) concentration, total thiol groups (TTG) content, superoxide dismutase (SOD), and catalase (CAT) activities were determined in the tissues.

RESULTS: In the experimental groups, MDA levels were significantly increased, while TTG, SOD, and CAT were significantly decreased in the total tissues of dams and their offspring.

CONCLUSION: Exposure to mobile phone (900-1800 MHz) during pregnancy induced oxidative stress in tissues of dams and their offspring.

<https://www.ncbi.nlm.nih.gov/pubmed/28434276>

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Pulsed or continuous EMF induce apoptotic signaling pathway in mouse spermatogenic cells in vitro and may affect male fertility

Solek P, Majchrowicz L, Bloniarz D, Krotoszynska E, Kozirowski M. Pulsed or continuous electromagnetic field induce p53/p21-mediated apoptotic signaling pathway in mouse spermatogenic cells in vitro and thus may affect male fertility. *Toxicology*. 2017 Mar 16. pii: S0300-483X(17)30092-6.

Abstract

The impact of electromagnetic field (EMF) on the human health and surrounding environment is a common topic investigated over the years. A significant increase in the electromagnetic field concentration arouses public concern about the long-term effects of EMF on living organisms associated with many aspects. In the present study, we investigated the effects of pulsed and continuous electromagnetic field (PEMF/CEMF) on mouse spermatogenic cell lines (GC-1 spg and GC-2 spd) in terms of cellular and biochemical features in vitro. We evaluated the effect of EMF on mitochondrial metabolism, morphology, proliferation rate, viability, cell cycle progression, oxidative stress balance and regulatory proteins. Our results strongly suggest that EMF induces oxidative and nitrosative stress-mediated DNA damage, resulting in p53/p21-dependent cell cycle arrest and apoptosis. Therefore, spermatogenic cells due to the lack of antioxidant enzymes undergo oxidative and nitrosative stress-mediated cytotoxic and genotoxic events, which contribute to infertility by reduction in healthy sperm cells pool. In conclusion, electromagnetic field present in surrounding environment impairs male fertility by inducing p53/p21-mediated cell cycle arrest and apoptosis.

<https://www.ncbi.nlm.nih.gov/pubmed/28323003>

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Mitochondrial DNA damage and oxidative damage in HL-60 cells exposed to 900MHz RF

Sun Y, Zong L, Gao Z, Zhu S, Tong J, Cao Y. Mitochondrial DNA damage and oxidative damage in HL-60 cells exposed to 900MHz radiofrequency fields. *Mutat Res*. 2017 Mar 7;797-799:7-14.

Abstract

HL-60 cells, derived from human promyelocytic leukemia, were exposed to continuous wave 900MHz radiofrequency fields (RF) at 120 μ W/cm² power intensity for 4h/day for 5 consecutive days to examine whether such exposure is capable damaging the mitochondrial DNA (mtDNA) mediated through the production of reactive oxygen species (ROS). In addition, the effect of RF exposure was examined on 8-hydroxy-2'-deoxyguanosine (8-OHdG) which is a biomarker for oxidative damage and on the mitochondrial synthesis of adenosine triphosphate (ATP) which is the energy required for cellular functions. The results indicated a significant increase in ROS

and significant decreases in mitochondrial transcription factor A, mtDNA polymerase gamma, mtDNA transcripts and mtDNA copy number in RF-exposed cells compared with those in sham-exposed control cells. In addition, there was a significant increase in 8-OHdG and a significant decrease in ATP in RF-exposed cells. The response in positive control cells exposed to gamma radiation (GR, which is also known to induce ROS) was similar to those in RF-exposed cells. Thus, the overall data indicated that RF exposure was capable of inducing mtDNA damage mediated through ROS pathway which also induced oxidative damage. Prior-treatment of RF- and GR-exposed the cells with melatonin, a well-known free radical scavenger, reversed the effects observed in RF-exposed cells.

<https://www.ncbi.nlm.nih.gov/pubmed/28340409>