

from the point of view of making sense of the brain impact of environmental challenges – including but not limited to EMF-RFR – this investigation is crucial.

The pathophysiological perspective that guides this review would suggest a move away from considering the behavioral manifestations of ASCs as core, intrinsic, ‘hard-wired traits.’ *Instead behaviors may be better understood as ‘outputs’ or emergent properties – what the brain and body produce – when their physiological attributes are altered* in these fashions for whatever reasons—be they genetic, environmental or many combinations of both [279–284]. Sleep and consciousness have also been considered ‘emergent properties’ [285,286]. Brain oscillatory activity is critical for organizing behavior, and it arises from cells and subcellular features that are shaped by the environment and can act differently based on their functional status as well as on account of external sensory or psychosocial stimuli.

In particular, (a) brain oscillatory activity is intimately connected with underlying cellular, metabolic and immune status, (b) EMF/RFR is capable of perpetrating changes at each of these levels, and (c) problems at each of these levels can make other problems worse. And as mentioned earlier, EMF/RFR and various toxicants can co-potentiate damage [287–294], amplifying ‘allostatic load’.

Put together, all of this implies that the combination of these EMF/RFR impacts may quite plausibly significantly contribute both to how ASCs happen in individuals and to why there are more reported cases of ASCs than ever before (1200–1500% increase in reported cases over the past 15–20 years, with studies showing that a substantial portion of this increase (45–65%) cannot be written off as artifact and may well represent true increases [295,296]).

The hopeful side of this framing of the problem comes from moving beyond the increasingly anachronistic idea that autism is determined overwhelmingly by genetic code about which we can do little or nothing. An emerging model that explains much more of what we now know frames ASCs as the dynamic, active outcomes of perturbed physiological processes – again, more like a chronic but changeable ‘state’ than a ‘trait.’ In the latter model, one is empowered – and motivated – to strongly reduce exposures and to make aggressive constructive environmental changes – particularly in diet and nutrition, given their protective potency discussed above [297]. In this way ‘allostatic load’ can be reduced, physiological damage can be repaired, homeostasis can be restored and resilience and optimal function can be promoted.

3. Implications

3.1. Exposures and their implications

Several thousand scientific studies over four decades point to serious biological effects and health harm from EMF and RFR [298,299]. These studies report genotoxicity, single-and double-strand DNA damage, chromatin condensation, loss

of DNA repair capacity in human stem cells, reduction in free-radical scavengers (particularly melatonin), abnormal gene transcription, neurotoxicity, carcinogenicity, damage to sperm morphology and function, effects on behavior, and effects on brain development in the fetus of human mothers that use cell phones during pregnancy. Cell phone exposure has been linked to altered fetal brain development and ADHD-like behavior in the offspring of pregnant mice [83].

3.1.1. Exposures have outpaced precautions

There is no question that huge new exposures to EMF/RFRs have occurred over the past few decades. As discussed extensively in the BioInitiative 2012 update [299], there is much concern that regulations to date have been based on a very limited sense of the pertinent biology, and particularly that limiting concern to thermal impacts is no longer valid since there is a wealth of evidence by now that non-thermal impacts can be biologically very powerful. Only in the last two decades have exposures to RFR and wireless technologies become so widespread as to affect virtually every living space, and affect every member of societies around the world. Even as some disease patterns like brain tumors from cell phone use have become ‘epidemiologically visible’, there are no comprehensive and systematic global health surveillance programs that really keep up to report EMF/RFR health trends [300].

The deployment of new technologies is running ahead of any reasonable estimation of possible health impacts and estimates of probabilities, let alone a solid assessment of risk. However, what has been missing with regard to EMF/RFR has been an acknowledgement of the risk that is demonstrated by the scientific studies. There is clear evidence of risk, although the magnitude of the risk is uncertain, and the magnitude of doing nothing on the health effects cost to society is similarly uncertain. This situation is very similar to our history of dealing with the hazards of smoking decades ago, where the power of the industry to influence governments and even conflicts of interest within the public health community delayed action for more than a generation, with consequent loss of life and enormous extra health care costs to society. [301].

3.1.2. The population’s exposure has increased

The very rapid global deployment of both old and new forms of emerging wireless technologies in the last two decades needs aggressive evaluation from a public health perspective, given the range of physiological impacts described in Section 2.

In the United States, the deployment of wireless infrastructure (cell tower sites) to support cell phone use has accelerated greatly in the last decades. The Cellular Telephone Institute of America (CTIA) estimated that in 1997 there were only 36,650 cell sites in the US; but increased rapidly to 131,350 in June 2002; 210,350 in June 2007 and 265,561 in June 2012 [302,303]. About 220,500 cell sites existed in 2008 [303–305]. These wireless facilities for cellular phone voice

and data transmission produce RFR over broad areas in communities and are an involuntary and unavoidable source of whole-body radiofrequency radiation exposure. Other new RFR exposures that did not exist before are from WI-FI access points (hotspots) that radiate 24/7 in cafes, stores, libraries, classrooms, on buses and trains, and from personal WI-FI enabled devices (iPads, tablets, PDAs, etc).

Not surprisingly, the use of cell phones has a parallel growth trend. In the late 1980s and early 1990's, only a few percent of the US population were cell phone users. By 2008, eighty-four percent (84%) of the population of the US owned cell phones. CTIA reports that wireless subscriber connections in the US increased from 49 million in June 1997 to 135 million in June 2002 to 243 million in June 2007 to 322 million in June 2012 [302,303]. This represents more than a 100% penetration rate in the US consumer market, up from just a few percent in the early 1990's. The number of wireless subscribers in June 1997 was 18%; in June 2002 it was 47%; in June 2007 it was 81% and in June 2012 it was 101%.

The annualized use of cell phones in the US was estimated to be 2.23 trillion minutes in 2008 and 2.296 trillion minutes in 2010 [303]. There are 6 billion users of cell phones worldwide in 2011 up from 2.2 billion in 2008 and many million more users of cordless phones.

The number of US homes with *only* wireless cell phones has risen from 10.5% in 2007 to 31.6% in June of 2012 [302,303]. There are no statistics for June 1997 nor for June 2002, since landline (non-wireless) phone use predominated. The shift to wireless communications, more minutes of use, and reliance on cell and cordless phones rather than corded phones is an extremely revealing measure of new EMF and RFR exposures for both adults and children.

The prevalence of autism has risen in parallel from one (1) in 5000 (1975) to 1 in 2500 (1985) to 1 in 500 (1995) to 1 in 250 (~2001) to 1 in 166 (~2004) to 1 in 88 (~2008) to 1 in 50 (~2013). All reflected birth cohorts born earlier^{1,2}. Further research into autism prevalence studies have debunked the initial contention that higher numbers could be explained away by better diagnosis and broadening of diagnostic criteria³⁻⁶.

3.1.3. Infants, children and childbearing families are highly exposed and vulnerable

The spread of cell towers in communities, often placed on pre-school, church day-care, and school campuses, means that young children may have hundreds of thousands of times higher RFR exposures in home and school environments than existed even 20–25 years ago. In addition, the nearly universal switch to cordless and cell phones, and away from corded landline phones, means that people are experiencing close and repetitive exposures to both EMF and RFR in the home [306]. Wireless laptops and wireless internet in schools, and home offices and for homework mean even more chronic exposures to RFR, a designated IARC 2B Possible Human Carcinogen [307,308]. The great utility of handheld devices as communication aids and engaging sources of information

and satisfaction for people on the autism spectrum may come with a concerning biologically harmful underbelly.

Exposures prior to conception or during pregnancy and infancy can come from faulty wiring, proximity to power lines, or high-frequency transients from a proximate transformer on a utility pole. Sources of pulsed RFR inside the home include an electronic baby monitor in the crib, a wireless router in the next room, a DECT phone that pulses high emissions of RFR on a continuous basis 24/7, or conversion to all compact fluorescent bulbs that produce significant 'dirty electricity' for occupants due to low-kilohertz frequency fields on electrical wiring and in ambient space. Sick and vulnerable infants in neonatal intensive care units are heavily exposed from being surrounded by equipment, with negative metabolic and autonomic consequences documented [32,258].

Wireless phones and laptops exposures produce extremely low frequency pulses from the battery of the wireless device [301,306,309] and the exposures to pulsed radiofrequency microwave radiation when the wireless device is transmitting or receiving calls and emails.

Especially since EMF/RFR exposures are already classified as IARC 2B Possible Human Carcinogens, we should be actively investigating these sources of damage to DNA that could reasonably result in 'de novo mutations' but also be aware that common environmental exposures from EMF and RFR might play a role in the higher rates of concordance for autism (ASD) among twins and siblings.

Researchers also should be aware that common environmental exposures from EMF and RFR might play a role in the higher rates of autism (ASD) among twins and siblings, not solely because of maternal use of wireless devices during pregnancy and paternal sperm exposure to wireless devices peri-conception; but also because such oxidative damage to DNA can occur at levels introduced into the world of the fetus, and young developing infant and child via baby surveillance monitoring devices in the crib and wireless devices in the home. The deployment of technologies poses risks to human fertility and reproduction capacity, to the fetus, to children and adults [301].

3.1.4. ASC risk and genomic damage to future generations

Barouki and Grandjean make a persuasive case that public health interventions are critically needed in early childhood development to prevent adult diseases that appear decades later [310]. Although they do not include EMF or RFR but only chemicals, they do say that physiological stressors, which EMF and RFR certainly have been established, should be reduced during critical development windows. They say: "*The current pandemic of non-communicable diseases and the increased prevalence of important dysfunctions demand an open interrogation of why current interventions appear insufficient. We now know that disease risk can be induced very early in the life course and that it is modifiable by*

nutrients and environmental chemical exposures (along with drugs, infections, and other types of stresses)” [310].

Public health interventions are warranted now to protect the genetic heritage of humans, as well as the other stocks of genetic material in wildlife and plants in the face of what appears to be on-going impairment of these genomes. The risk of genomic damage for future generations is sufficiently documented to warrant strong preventative action and new public safety limits that observe EMF/RFR levels shown to cause adverse effects.

3.1.5. De-tuning the organism

Genetic mutations may lead to cancer and other diseases in the present and future generations, but the exposures that are capable of creating genotoxic impacts also compromise physiological function. Even genotoxicity can have not only specific but also non-specific effects due to molecular inefficiencies, misfolded proteins, and cellular debris [311,312].

In the setting of autism, a baby gestated or developing as a neonate in a milieu with excessively elevated EMF/RFR exposures is vulnerable to interference with the normal development processes, including the organization of information and experience in the brain. This baby's environment also often includes nutritional insufficiencies (processed denatured pesticide-laden food low in antioxidants, minerals and essential fatty acids essential to cellular protection). The baby's gestational period may have been complicated by the mother's own health issues such as conditions like obesity and diabetes [313] which converge upon on inflammation, oxidative stress and other common forms of physiological dysregulation. The exquisite 'tuning up' of the brain and body as it develops will integrate and respond to the environmental inputs it receives, and is particularly sensitive to environmental miscues (whether chemical like endocrine disruptors, EMF/RFR which can be both chemically and electromagnetically disruptive, or other environmental conditions whether hostile or nurturing). To the extent that the baby is burdened with more disorganized or hostile cues than nurturing and organizing cues, that baby may lose resiliency and become more physiologically vulnerable –perhaps approaching a tipping point into decompensation such as autistic regression or development of other chronic disease processes.

From a systems point of view, the phenomenon of 'autistic regression' can be understood as occurring after an accumulation of multisystem signaling interference leading to a tipping point of loss of some vital systems synchronization and increase in randomization. EMF/RFR exposures could plausibly contribute both to this vulnerability and to the decompensation/desynchronization process – as could other stressors such as infection, toxicity, acute stress. The vulnerability, then, is the 'allostatic load' – the total burden of stressors pressing toward disorganization. The tipping point may come in a variety of ways; but upon investigation one is likely to find that unless a stressor is severe, the trigger most proximally associated with the decompensation is likely to

be the 'straw that breaks the camel's back' laid atop a prior accumulation of 'allostatic load.'

3.2. Conclusions and recommendations

The case has been made that ASCs involve physiological challenges at multiple levels, and that these challenges are paralleled in the physiological impacts of EMF/RFR exposure. Evidence has also been presented to suggest that the many levels of damage and degradation of physiological and functional integrity are profoundly related to each other. Although autism spectrum conditions (ASCs) are defined by problems with behavior, communication, social interaction and sensory processing, under the surface they also involve a range of disturbances of underlying biology that find striking parallels in the physiological impacts of electromagnetic frequency and radiofrequency radiation exposures (EMF/RFR). At the cellular and molecular level many studies of people with ASCs have identified oxidative stress and evidence of free radical damage, evidence of cellular stress proteins, as well as deficiencies of antioxidants such as glutathione. Elevated intracellular calcium in ASCs can be associated with genetic mutations but more often may be downstream of inflammation or chemical exposures. Cell membrane lipids may be peroxidized, mitochondria may function poorly, and immune system disturbances of various kinds are common. Brain oxidative stress and inflammation as well as measures consistent with blood–brain barrier and brain perfusion compromise have been documented. Changes in brain and autonomic nervous system electrophysiology can be measured and seizures are far more common than in the population at large. Sleep disruption and high levels of stress are close to universal. In parallel, all of these phenomena have also been documented to result from or be modulated by EMF/RFR exposure. Moreover, some people with ASCs have de novo mutations (that their parents do not have), and EMF/RFR exposures could contribute to this due to their potential genotoxicity. EMF/RFR exposure during pregnancy may send spurious signals to developing brain cells during pregnancy, altering brain development during critical periods, and may increase oxidative stress and immune reactivity that can increase risk for later developmental impairments, with further disruption later in development increasing risk, physiological dysregulation and severity of outcome.

All of this does not prove that EMF/RFR exposures cause autism, but it does raise concerns that they could contribute by increasing risk, and by making challenging biological problems and symptoms worse in these vulnerable individuals. Placed alongside the dramatic rise in reported cases of ASCs [333], that parallels the dramatic rise in deployment of wireless technologies, a strong case can be made for aggressively investigating links between ASCs and EMR/RFR, and minimizing exposures for people with autism as well as families preconceptionally, during pregnancy, and around infants and children at home, at school, and in health care centers and hospitals.

These arguments have implications for how we understand what ASCs ‘are’ and how they work, including an appreciation that it may be the physiological disturbance is what actually generates the ‘autism’ on a moment-to-moment basis—and that these physiological disturbances are profoundly driven by environmental insults. These implications call upon us to take the environmental contribution very seriously, which involves on the one hand a sobering appreciation of the vast array of exposures that can contribute to risk via perturbed development and physiological degradation, and on the other hand a sense that there are powerful things we can do to reduce risk and improve the situation.

3.2.1. Change our deployment of EMF/RFR

The deployment of RFR from wireless technologies has incredible momentum, and it has made many things easier and many other things possible for the first time. On the other hand this momentum can interfere with setting up the technology in a fashion truly respectful of biological tolerances. *“There is no question that global implementation of the safety standards proposed in the Bioinitiative (2007) Report, if implemented abruptly and without careful planning, have the potential to not only be very expensive but also disruptive of life and the economy as we know it. Action must be a balance of risk to cost to benefit. The major risk from maintaining the status quo is an increasing number of cancer cases, especially in young people, as well as neurobehavioral problems at increasing frequencies. The benefits of the status quo are expansion and continued development of communication technologies. But we suspect that the true costs of even existing technologies will only become much more apparent with time. Whether the costs of remedial action are worth the societal benefits is a formula that should reward precautionary behavior”* [301].

3.2.2. Encourage precautions right now based on present knowledge

Physicians and health care workers should raise the visibility of EMF/RFR as a plausible environmental factor in clinical evaluations and treatment protocols. Reducing or removing EMF and wireless RFR stressors from the environment is a reasonable precautionary action given the overall weight of evidence.

- Children with existing neurological problems that include cognitive, learning, attention, memory, or behavioral problems should as much as possible be provided with wired (not wireless) learning, living and sleeping environments,
- Special education classrooms should aim for ‘no wireless’ conditions to reduce avoidable stressors that may impede social, academic and behavioral progress.
- Adaptations to preserve the attractive design innovations of technologies such as tablet computers in a ‘no wireless’ environment should be developed.

- All children should reasonably be protected from the physiological stressor of significantly elevated EMF/RFR (wireless in classrooms, or home environments).
- School districts that are now considering all-wireless learning environments should be strongly cautioned that wired environments are likely to provide better learning and teaching environments, and prevent possible adverse health consequences for both students and faculty in the long-term.
- Monitoring of the impacts of wireless technology in learning and care environments should be performed with sophisticated measurement and data analysis techniques that are cognizant of the non-linear impacts of EMF/RFR and of data techniques most appropriate for discerning these impacts.
- There is sufficient scientific evidence to warrant the selection of wired internet, wired classrooms and wired learning devices, rather than making an expensive and potentially health-harming commitment to wireless devices that may have to be substituted out later, and
- Wired classrooms should reasonably be provided to all students who opt-out of wireless environments.

Broader recommendations also apply, related to reducing the physiological vulnerability to exposures, reduce ‘allostatic load’ and build physiological resiliency through high quality nutrition, reducing exposure to toxicants and infectious agents, and reducing stress [297], all of which can be implemented safely based upon presently available knowledge.

3.2.3. Build an environmentally physiologically centered research program in ASCs as a platform for investigating the EMR/RFR-ASC linkage

This review has been structured around the physiological parallels between ASCs and the impacts of EMF/RFR. What is missing from the autism research agenda is some cross-study of these two bodies of research evidence. To do this we will need both a recognition of the importance of these risks, and a collaborative multi-site research program centered around a “middle-out” physiological approach [314] that can transcend the limits of the gene-brain-behavior agenda that has dominated ASC research, by incorporating this now clearly limited approach into a broader framework [315]. This still dominant gene-brain-behavior approach has been based on an expectation of linear mapping across the levels on which it focuses, but instead the systems involved appear to be much more complex. The middle-out approach is an emerging more inclusive framework in systems biology that can incorporate complexity and nonlinear, multi-scale modeling [316–320]. The physiological levels largely left out in the gene-only approach are critically important to helping people with ASCs because they will help not only with understanding how environment impacts function but also with identifying leverage points.

3.2.4. Take the evidence as a call to action

Both EMF and RFR exposures are already classified as IARC Group 2B Possible Human Carcinogens. The substantial scientific literature on EMF and RFR effects on DNA, on immune and blood–brain barrier disruption, on stress proteins, on circadian rhythms and hormone dysregulation, and on cognition, sleep, disruption of neural control and altered brainwave activity all argue for reduction of exposures now, and better coordinated research in these areas. The evidence is sufficiently documented to warrant strong preventative action and new public safety limits that observe EMF/RFR levels shown to cause adverse effects.

All relevant environmental conditions should be given weight in defining and implementing prudent, precautionary actions to protect public health, including EMF and RFR. Evidence is sufficient to add EMF/RFR prominently to the list of exposures that can degrade the human genome, and impair normal development, health and quality of our physiology. With the rising numbers people with ASCs and other childhood health and developmental disorders, we cannot afford to ignore this component of risk to our children and vulnerable populations. When the risk factors are largely avoidable or preventable, ignoring clear evidence of large-scale health risks to global populations poses unnecessary and unacceptable risks. Taking this evidence as a call to action will be challenging and disruptive in the short term, but constructive in the longer term as we learn to use EMF/RFR in healthier ways.

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Fertility; Research Abstracts, List of References Reporting Fertility and/
or Reproduction Effects from Electromagnetic Fields and/or
Radiofrequency Radiation (66 references)

List of References Reporting Fertility and/or Reproduction Effects from Electromagnetic Fields and/or Radiofrequency Radiation (66 references)

(with abstracts)

Agarwal A, Deepinder F, Sharma RK, Ranga G, Li J. (2008) Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study. Fertility and Sterility 89(1):124-8.

OBJECTIVE: To investigate the effect of cell phone use on various markers of semen quality.

DESIGN: Observational study.

SETTING: Infertility clinic.

PATIENT(S): Three hundred sixty-one men undergoing infertility evaluation were divided into four groups according to their active cell phone use: group A: no use; group B: <2 h/day; group C: 2-4 h/day; and group D: >4 h/day.

INTERVENTION(S): None.

MAIN OUTCOME MEASURE(S): Sperm parameters (volume, liquefaction time, pH, viscosity, sperm count, motility, viability, and morphology).

RESULT(S): The comparisons of mean sperm count, motility, viability, and normal morphology among four different cell phone user groups were statistically significant. Mean sperm motility, viability, and normal morphology were significantly different in cell phone user groups within two sperm count groups. The laboratory values of the above four sperm parameters decreased in all four cell phone user groups as the duration of daily exposure to cell phones increased.

CONCLUSION(S): Use of cell phones decrease the semen quality in men by decreasing the sperm count, motility, viability, and normal morphology. The decrease in sperm parameters was dependent on the duration of daily exposure to cell phones and independent of the initial semen quality.

**(Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, Sabanegh E, Sharma R)
Agarwal A, Desai NR, Makker K, et al. (2009) Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. Fertility and Sterility 92(4):1318-25.**

OBJECTIVE: To evaluate effects of cellular phone radiofrequency electromagnetic waves (RF-EMW) during talk mode on unprocessed (neat) ejaculated human semen.

DESIGN: Prospective pilot study.

SETTING: Center for reproductive medicine laboratory in tertiary hospital setting.

SAMPLES: Neat semen samples from normal healthy donors (n = 23) and infertile patients (n = 9).

INTERVENTION(S): After liquefaction, neat semen samples were divided into two aliquots. One aliquot (experimental) from each patient was exposed to cellular phone radiation (in talk mode) for 1 h, and the second aliquot (unexposed) served as the control sample under identical conditions.

MAIN OUTCOME MEASURE(S): Evaluation of sperm parameters (motility, viability), reactive oxygen species (ROS), total antioxidant capacity (TAC) of semen, ROS-TAC score, and sperm DNA damage.

RESULT(S): Samples exposed to RF-EMW showed a significant decrease in sperm motility and viability, increase in ROS level, and decrease in ROS-TAC score. Levels of TAC and DNA damage showed no significant differences from the unexposed group.

CONCLUSION(S): Radiofrequency electromagnetic waves emitted from cell phones may lead to oxidative stress in human semen. We speculate that keeping the cell phone in a trouser pocket in talk mode may negatively affect spermatozoa and impair male fertility.

Agarwal A, Desai NR, Ruffoli R, Carpi A. (2008) Lifestyle and testicular dysfunction: a brief update. Biomed Pharmacother. 62(8):550-3.

The incidence of testicular cancer, cryptorchidism and defective spermatogenesis is increasing probably due to environmental and lifestyle-related factors. The aim of this review is to briefly describe and comment on the principal lifestyle factors. The recent findings that the electromagnetic waves following the use of the cell phone and the prolonged exposure to the noise stress cause relevant testicular dysfunction in man or animals reinforce the hypothesis of the importance of lifestyle-related factors.

Agarwal A, Singh A, Hamada A, Kesari K (2011) Cell phones and male infertility: a review of recent innovations in technology and consequences. Brazilian Journal of Urology 37(4):432-54.

Cell phones have become a vital part of everyday life. However, the health risks associated with their usage are often overlooked. Recently, evidence from several studies supports a growing claim that cell phone usage may have a detrimental effect on sperm parameters leading to decreased male fertility. Nonetheless, other studies showed no conclusive link between male infertility and cell phone usage. The ambiguity of such results is attributed to the lack of a centralized assay for measuring inflicted damage caused by cell phones. Study design, ethics, and reproducibility are all aspects which must be standardized before any conclusions can be made.

Aitken RJ, Bennetts LE, Sawyer D, Wiklendt AM, King BV (2005) Impact of radio frequency electromagnetic radiation on DNA integrity in the male germline. International Journal of Andrology 28(3):179-179.

Concern has arisen over human exposures to radio frequency electromagnetic radiation (RFEMR), including a recent report indicating that regular mobile phone use can negatively impact upon human semen quality. These effects would be particularly serious if the biological effects of RFEMR included the induction of DNA damage in male germ cells. In this study, mice were exposed to 900 MHz RFEMR at a specific absorption rate of approximately 90 mW/kg inside a waveguide for 7 days at 12 h per day. Following exposure, DNA damage to caudal epididymal spermatozoa was assessed by quantitative PCR (QPCR) as well as alkaline and pulsed-field gel electrophoresis. The treated mice were overtly normal and all assessment criteria, including sperm number, morphology and vitality were not significantly affected. Gel electrophoresis revealed no gross evidence of increased single- or double-DNA strand breakage in spermatozoa taken from treated animals. However, a detailed analysis of DNA integrity using QPCR revealed statistically significant damage to both the mitochondrial genome ($p < 0.05$) and the nuclear beta-globin locus ($p < 0.01$). This study suggests that while RFEMR does not have a dramatic impact on male germ cell development, a significant genotoxic effect on epididymal spermatozoa is evident and deserves further investigation.

Avendaño C, Mata A, Sanchez Sarmiento CA, Doncel GF (2012) Use of laptop computers connected to internet through Wi-Fi decreases human sperm motility and increases sperm DNA fragmentation. Fertility and Sterility [Epub ahead of print]

OBJECTIVE: To evaluate the effects of laptop computers connected to local area networks wirelessly (Wi-Fi) on human spermatozoa.

DESIGN: Prospective in vitro study.

SETTING: Center for reproductive medicine.

PATIENT(S): Semen samples from 29 healthy donors.

INTERVENTION(S): Motile sperm were selected by swim up. Each sperm suspension was divided into two aliquots. One sperm aliquot (experimental) from each patient was exposed to an internet-connected laptop by Wi-Fi for 4 hours, whereas the second aliquot (unexposed) was used as control, incubated under identical conditions without being exposed to the laptop.

MAIN OUTCOME MEASURE(S): Evaluation of sperm motility, viability, and DNA fragmentation.

RESULT(S): Donor sperm samples, mostly normozoospermic, exposed ex vivo during 4 hours to a wireless internet-connected laptop showed a significant decrease in progressive sperm motility and an increase in sperm DNA fragmentation. Levels of dead sperm showed no significant differences between the two groups.

CONCLUSION(S): To our knowledge, this is the first study to evaluate the direct impact of laptop use on human spermatozoa. Ex vivo exposure of human spermatozoa to a wireless internet-connected laptop decreased motility and induced DNA fragmentation by a nonthermal effect. We speculate that keeping a laptop connected wirelessly to the internet on the lap near the testes may result in decreased male fertility. Further in vitro and in vivo studies are needed to prove this contention.

Awad H, Halawa F, Mostafa T, Atta H. (2006) Melatonin hormone profile in infertile males. International Journal of Andrology 29(3):409-13.

Melatonin is a hormone produced by the pineal gland. There is much controversy about its relationship to the male reproductive process. In this study, seminal plasma as well as the serum melatonin levels were studied in different infertile male groups and were correlated with their semen parameters and hormonal levels. One hundred twenty male cases subdivided into six equal groups were consecutively included; fertile normozoospermic men, oligoasthenozoospermia (OA), OA with leucocytospermia, OA with varicocele, non-obstructive azoospermia (NOA) with high serum follicle stimulating hormone (FSH) and NOA with normal FSH. Semen analysis, estimation of melatonin, FSH, testosterone (T) and prolactin (PRL) hormone was carried out. Mean level of serum melatonin was higher than its corresponding seminal concentrations in all investigated groups with a positive correlation between their levels ($r = 0.532$, $p = 0.01$). Serum and seminal plasma melatonin levels in all infertile groups were reduced significantly compared with their levels in the fertile group. The lowest concentrations were in OA with leucocytospermia group. Melatonin in both serum and semen demonstrated significant correlation with sperm motility ($r = 0.607$, 0.623 respectively, $p = 0.01$). Serum melatonin correlated positively with serum PRL ($r = 0.611$, $p = 0.01$). It may be concluded that melatonin may be involved in the modulation of reproductive neuroendocrine axis in male infertility. Also, low levels of melatonin in semen were observed in infertile groups having reduced sperm motility, leucocytospermia, varicocele and NOA.

Balmori A (2009) Electromagnetic pollution from phone masts. Effects on wildlife. Pathophysiology 16(2-3):191-9.

A review on the impact of radiofrequency radiation from wireless telecommunications on wildlife is presented. Electromagnetic radiation is a form of environmental pollution which may hurt wildlife. Phone masts located in their living areas are irradiating continuously some species that could suffer long-term effects, like reduction of their natural defenses, deterioration of their health, problems in reproduction and reduction of their useful territory through habitat deterioration. Electromagnetic radiation can exert an aversive behavioral response in rats, bats and birds such as sparrows. Therefore microwave and radiofrequency pollution constitutes a potential cause for the decline of animal populations and deterioration of health of plants living near phone masts. To measure these effects urgent specific studies are necessary.

Baste V, Riise T, Moen BE (2008) Radiofrequency electromagnetic fields; male infertility and sex ratio of offspring. European Journal of Epidemiology 23(5):369-77.

Concern is growing about exposure to electromagnetic fields and male reproductive health. The authors performed a cross-sectional study among military men employed in the Royal Norwegian Navy, including information about work close to equipment emitting radiofrequency electromagnetic fields, one-year infertility, children and sex of the offspring. Among 10,497 respondents, 22% had worked close to high-frequency aerials to a "high" or "very high" degree. Infertility increased significantly along with increasing self-reported exposure to radiofrequency electromagnetic fields. In a logistic regression, odds ratio (OR) for infertility among those who had

worked closer than 10 m from high-frequency aeriels to a "very high" degree relative to those who reported no work near high-frequency aeriels was 1.86 (95% confidence interval (CI): 1.46-2.37), adjusted for age, smoking habits, alcohol consumption and exposure to organic solvents, welding and lead. Similar adjusted OR for those exposed to a "high", "some" and "low" degree were 1.93 (95% CI: 1.55-2.40), 1.52 (95% CI: 1.25-1.84), and 1.39 (95% CI: 1.15-1.68), respectively. In all age groups there were significant linear trends with higher prevalence of involuntary childlessness with higher self-reported exposure to radiofrequency fields. However, the degree of exposure to radiofrequency radiation and the number of children were not associated. For self-reported exposure both to high-frequency aeriels and communication equipment there were significant linear trends with lower ratio of boys to girls at birth when the father reported a higher degree of radiofrequency electromagnetic exposure.

Behari J, Kesari KK (2006) Effects of microwave radiations on reproductive system of male rats. Embryo Talk 1 (Suppl.1):81-5.

Recently, there have been reports referring to studies on health effects due to exposure of radiofrequency electromagnetic radiation (RFEMR). In this context mobile phones are often being implicated. In an attempt to quantitate this study was undertaken to examine their exposure effects. Animals were exposed continuously to 900 MHz Frequency at a specific absorption rate of approximately 0.9 W/Kg for 35 days at 2 hours per day. Rats were placed in Plexiglas cages with drilled ventilation holes, which have been attached with mobile phone hand set. After the exposure period, rats were immediately sacrificed and sperms were collected for the study of DNA double strand breaks by microgel electrophoresis (Comet assay), sperm count and testis weight was taken. To confirm this at other frequencies animals were exposed to low intensity microwaves (2.45 GHz, 0.34 mW/cm² SAR 0.1 W/Kg). A similar set of studies was undertaken after the exposure period, when the animals were similarly sacrificed. Results obtained using the mobile phone exposure shows that the chronic exposure to these radiations cause double strand DNA breaks in sperm cells. This study also shows that the mobile radiation exposure can cause statistically significant decrease in the sperm count and testes weight. A similar set of data was obtained from 2.45 GHz exposure. It is concluded that microwave induced effects on reproductive system are uniformly distributed over the electromagnetic spectrum under investigation.

Belyaev IY, Grigoriev YG (2007) Problems in assessment of risks from exposures to microwaves of mobile communication. Radiatsionnaia biologii, radioecologii / Rossiiskaia akademiia nauk 47(6):727-32.

Since pioneering investigations published in the beginning of 1970th, various biological responses to non-thermal (NT) microwaves (MW), including adverse health effects, have been described by many research groups all over the world. There is strong evidence that the NT MW biological effects depend on several physical parameters and biological variables, which must be controlled in replication studies. Apart from the fundamental importance, the development of comprehensive mechanisms for the NT MW effects is socially important. The effects of MW of mobile communications are of major concern because of the increased exposure in many countries. It has been shown that adverse effects of NT MW from GSM/UMTS mobile phones on human lymphocytes from healthy and hypersensitive to EMF persons depend on carrier frequency and modulation. Further investigations with human primary cells, animals and volunteers are needed to elucidate possible adverse effects of MW signals that are used in wireless communication. Identification of those types and frequency channels/bands for mobile communication, which do not affect human cells, is urgently needed as the high priority task for the development of safe mobile communication. Numerous data on the NT MW effects clearly indicate that the SAR-concept alone cannot underlie the safety guidelines for chronic exposures to MW from mobile communication and other approaches are needed. However, there is not enough research information to set exposure MW standards. Various genetic and epigenetic effects of signals used in mobile communication should be studied. It has been shown that NT MW affect cells of various types including stem cells and reproductive organs. Stem cells represent especially important cellular model because recent data suggest that different cancer types, including leukemia, have a fundamentally common basis that is grounded on epigenetic changes in stem cells.

Blank M, Goodman R (2011) DNA is a fractal antenna in electromagnetic fields. International Journal of Radiation Biology 87(4):409-15.

PURPOSE: To review the responses of deoxyribonucleic acid (DNA) to electromagnetic fields (EMF) in different frequency ranges, and characterise the properties of DNA as an antenna.

MATERIALS AND METHODS: We examined published reports of increased stress protein levels and DNA strand breaks due to EMF interactions, both of which are indicative of DNA damage. We also considered antenna properties such as electronic conduction within DNA and its compact structure in the nucleus.

RESULTS: EMF interactions with DNA are similar over a range of non-ionising frequencies, i.e., extremely low frequency (ELF) and radio frequency (RF) ranges. There are similar effects in the ionising range, but the reactions are more complex.

CONCLUSIONS: The wide frequency range of interaction with EMF is the functional characteristic of a fractal antenna, and DNA appears to possess the two structural characteristics of fractal antennas, electronic conduction and self symmetry. These properties contribute to greater reactivity of DNA with EMF in the environment, and the DNA damage could account for increases in cancer epidemiology, as well as variations in the rate of chemical evolution in early geologic history.

Davoudi M, Brossner C, Kuber W (2002) Der Einfluelektromagnetischer Wellen auf die Spermienmotilit. Journal Für Urologie Und Urogynäkologie 9(3):18-22.

Objective: To evaluate the influence of electromagnetic waves (EMW) caused by mobile phones on sperm motility.

Methods: 13 men with a normal spermiogramm regarding the WHO criteria were included in our study. After a GSM-mobile phone was not carried or used during 5 days a first spermiogramm was analysed. Four weeks later, a second spermiogramm was performed. Five days before this second spermiogramm, men carried the mobile phone on the belt and used it 6 hours a day intensively. Spermiogramm parameters of the first and second spermiogramm were compared.

Results: Rapid progressive spermatozoa were reduced significantly in the second spermiogramm compared to the first. Decrease was from (mean) 32.3 % (SD $\pm$ 6.13) to (mean) 26.1 % (SD $\pm$ 6.5), $p = 0.0004$. In addition there was a shift to an increase of progressive spermatozoa from mean 24.8 % (SD $\pm$ 3.62) to 29.7 % (SD $\pm$ 6.11), $p = 0.01$. All other spermiogramm parameters like semen volume, density and morphology did not differ significantly.

Conclusion: Our data suggest a decreased motility of rapid progressive spermatozoa caused by electromagnetic waves of GSM-mobile phones. These findings may have an impact in counselling subfertile men.

Deepinder F, Makker K, Agarwal A (2007) Cell phones and male infertility: dissecting the relationship. Reproductive Biomedicine Online 15(3):266-70.

There has been a tremendous increase in the use of mobile phones in the past decade and concerns are growing about the possible hazardous effects of radio-frequency electromagnetic waves (EMW) emitted by these devices on human health. Preliminary studies, though with limitations in study design, suggest a possible link between cell phone use and infertility. A recent study found that use of cell phones adversely affects the quality of semen by decreasing the sperm counts, motility, viability and morphology. Evidence of detrimental effect of mobile phones on male fertility is still equivocal as studies have revealed a wide spectrum of possible effects ranging from insignificant effects to variable degrees of testicular damage. Although previous studies suggested a role of cell phone use in male infertility, the mode of action of EMW emitted from cell phones on the male reproductive system is still unclear. EMW can affect the reproductive system via an EMW-specific effect, thermal molecular effect or combination of both. Studies performed on human males are scarce and therefore further studies with a careful design are needed to determine the effect of cell phone use on male-fertilizing potential.

De Iuliis GN, Newey RJ, King BV, Aitken RJ (2009) Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. PLoS One 4(7):e6446.

BACKGROUND: In recent times there has been some controversy over the impact of electromagnetic radiation on human health. The significance of mobile phone radiation on male reproduction is a key element of this debate since several studies have suggested a relationship between mobile phone use and semen quality. The potential mechanisms involved have not been established, however, human spermatozoa are known to be particularly vulnerable to oxidative stress by virtue of the abundant availability of substrates for free radical attack and the lack of cytoplasmic space to accommodate antioxidant enzymes. Moreover, the induction of oxidative stress in these cells not only perturbs their capacity for fertilization but also contributes to sperm DNA damage. The latter has, in turn, been linked with poor fertility, an increased incidence of miscarriage and morbidity in the offspring, including childhood cancer. In light of these associations, we have analyzed the influence of RF-EMR on the cell biology of human spermatozoa in vitro.

PRINCIPAL FINDINGS: Purified human spermatozoa were exposed to radio-frequency electromagnetic radiation (RF-EMR) tuned to 1.8 GHz and covering a range of specific absorption rates (SAR) from 0.4 W/kg to 27.5 W/kg. In step with increasing SAR, motility and vitality were significantly reduced after RF-EMR exposure, while the mitochondrial generation of reactive oxygen species and DNA fragmentation were significantly elevated ($P < 0.001$). Furthermore, we also observed highly significant relationships between SAR, the oxidative DNA damage bio-marker, 8-OH-dG, and DNA fragmentation after RF-EMR exposure.

CONCLUSIONS: RF-EMR in both the power density and frequency range of mobile phones enhances mitochondrial reactive oxygen species generation by human spermatozoa, decreasing the motility and vitality of these cells while stimulating DNA base adduct formation and, ultimately DNA fragmentation. These findings have clear implications for the safety of extensive mobile phone use by males of reproductive age, potentially affecting both their fertility and the health and wellbeing of their offspring.

Desai NR, Kesari KK, Agarwal A (2009) Pathophysiology of cell phone radiation: oxidative stress and carcinogenesis with focus on male reproductive system. Reproductive Biology and Endocrinology 7:114.

Hazardous health effects stemming from exposure to radiofrequency electromagnetic waves (RF-EMW) emitted from cell phones have been reported in the literature. However, the cellular target of RF-EMW is still controversial. This review identifies the plasma membrane as a target of RF-EMW. In addition, the effects of RF-EMW on plasma membrane structures (i.e. NADH oxidase, phosphatidylserine, ornithine decarboxylase) and voltage-gated calcium channels are discussed. We explore the disturbance in reactive oxygen species (ROS) metabolism caused by RF-EMW and delineate NADH oxidase mediated ROS formation as playing a central role in oxidative stress (OS) due to cell phone radiation (with a focus on the male reproductive system). This review also addresses: 1) the controversial effects of RF-EMW on mammalian cells and sperm DNA as well as its effect on apoptosis, 2) epidemiological, in vivo animal and in vitro studies on the effect of RF-EMW on male reproductive system, and 3) finally, exposure assessment and dosimetry by computational biomodeling.

(Erogul O, Oztas E, Yildirim I, Kir T, Aydur E, Komesli G, Irkilata HC, Irmak MK, Peker AF) Erogul O, Oztas E, Yildirim I, et al. (2006) Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study. Archives of Medical Research 37(7):840-3.

BACKGROUND: There has been growing public concern on the effects of electromagnetic radiation (EMR) emitted by cellular phones on human health. Many studies have recently been published on this topic. However, possible consequences of the cellular phone usage on human sperm parameters have not been investigated adequately.

METHODS: A total number of 27 males were enrolled in the study. The semen sample obtained from each participant was divided equally into two parts. One of the specimens was exposed to EMR emitted by an activated 900 MHz cellular phone, whereas the other was not. The concentration and motility of the specimens were compared to analyze the effects of EMR. Assessment of sperm movement in all specimens was performed using four criteria: (A) rapid progressive, (B) slow progressive, (C) nonprogressive, (D) no motility.

RESULTS: Statistically significant changes were observed in the rapid progressive, slow progressive and no-motility categories of sperm movement. EMR exposure caused a subtle decrease in the rapid progressive and slow progressive sperm movement. It also caused an increase in the no-motility category of sperm movement. There was no statistically significant difference in the sperm concentration between two groups.

CONCLUSIONS: These data suggest that EMR emitted by cellular phone influences human sperm motility. In addition to these acute adverse effects of EMR on sperm motility, long-term EMR exposure may lead to behavioral or structural changes of the male germ cell. These effects may be observed later in life, and they are to be investigated more seriously.

Falzone N, Huyser C, Franken DR, Leszczynski D (2010) Mobile phone radiation does not induce pro-apoptosis effects in human spermatozoa. Radiation Research 174(2):169-76.

Recent reports suggest that mobile phone radiation may diminish male fertility. However, the effects of this radiation on human spermatozoa are largely unknown. The present study examined effects of the radiation on induction of apoptosis-related properties in human spermatozoa. Ejaculated, density-purified, highly motile human spermatozoa were exposed to mobile phone radiation at specific absorption rates (SARs) of 2.0 and 5.7 W/kg. At various times after exposure, flow cytometry was used to examine caspase 3 activity, externalization of phosphatidylserine (PS), induction of DNA strand breaks, and generation of reactive oxygen species. Mobile phone radiation had no statistically significant effect on any of the parameters studied. This suggests that the impairment of fertility reported in some studies was not caused by the induction of apoptosis in spermatozoa.

Falzone N, Huyser C, Becker P, Leszczynski D, Franken DR (2010) The effect of pulsed 900-MHz GSM mobile phone radiation on the acrosome reaction, head morphometry and zona binding of human spermatozoa. International Journal of Andrology 33:1-7.

Falzone N, Huyser C, Becker P, Leszczynski D, Franken DR (2011) The effect of pulsed 900-MHz GSM mobile phone radiation on the acrosome reaction, head morphometry and zona binding of human spermatozoa. International Journal of Andrology 34(1):20-6.

Several recent studies have indicated that radiofrequency electromagnetic fields (RF-EMF) have an adverse effect on human sperm quality, which could translate into an effect on fertilization potential. This study evaluated the effect of RF-EMF on sperm-specific characteristics to assess the fertilizing competence of sperm. Highly motile human spermatozoa were exposed for 1 h to 900-MHz mobile phone radiation at a specific absorption rate of 2.0 W/kg and examined at various times after exposure. The acrosome reaction was evaluated using flow cytometry. The radiation did not affect sperm propensity for the acrosome reaction. Morphometric parameters were assessed using computer-assisted sperm analysis. Significant reduction in sperm head area ($9.2 \pm 0.7 \mu\text{m}^2$ vs. $18.8 \pm 1.4 \mu\text{m}^2$) and acrosome percentage of the head area ($21.5 \pm 4\%$ vs. $35.5 \pm 11.4\%$) was reported among exposed sperm compared with unexposed controls. Sperm-zona binding was assessed directly after exposure using the hemizona assay. The mean number of zona-bound sperm of the test hemizona and controls was 22.8 ± 12.4 and 31.8 ± 12.8 ($p < 0.05$), respectively. This study concludes that although RF-EMF exposure did not adversely affect the acrosome reaction, it had a significant effect on sperm morphometry. In addition, a significant decrease in sperm binding to the hemizona was observed. These results could indicate a significant effect of RF-EMF on sperm fertilization potential.

Fejes I, Závaczki Z, Szöllosi J, Koloszar S, Kovacs L, Pal A (2004) Relationship between regular cell phone use and human semen quality. Abstracts of the 20th Annual Meeting of the ESHRE, Berlin, Germany, 27–30 June 2004.

Introduction: Environmental factors can be responsible for the deteriorative sperm parameters detected in the last decades. The effects of the electromagnetic field of mobile phones (900MHz) on human spermatogenesis have not been studied yet. Our aim was to determine possible relationship between regular cell phone use and the different human semen attributes.

Methods: Localisation: University of Szeged, Dept. Obstetrics and Gynaecology, Hungary. History taking was supplemented with questions, how long patient owns mobile phone, how long it is standby in a day (in hours) near the patient, and how long it transmits daily (in minutes). Semen analyses were performed using Makler sperm counting chamber. Sperm concentration, motility according to WHO guidelines, motile sperm count and progressively motile sperm count were assessed. Comparison between non-users and very active users has been drawn. Statistical analyses were performed using SPSS 11.0 software.

Results: A total of 451 patients were examined during the 13 months of study period. Among the 221 men corresponded the criteria and completed the study, significant correlations were found between duration of standby position and sperm concentration ($r=-0.161$, $p=0.04$) length of daily transmission and rapid progressive or slow progressive motility ($r=-0.191$, $p=0.005$; $r=0.323$, $p<0.001$, respectively) and between the duration of standby position and rapid progressive motile sperm concentration ($r=-0.218$, $p=0.005$). Furthermore, difference was found between daylong standby and non-standby users in sperm concentration ($59.11 \times 10^6/\text{ml}$ vs $82.97 \times 10^6/\text{ml}$, $p=0.021$, $N=51$ vs 46) and between prolonged transmitters and non-transmitters in rapid progressive motility (36.31% vs 51.34% , $p=0.007$, $N=16$ vs 61). Conclusions: The prolonged use of cell phones may have negative effect on spermatogenesis and male fertility, that presumably deteriorates both concentration and motility. Further controlled randomised studies are necessary to percise the correlation coefficients.

(Fejes I, Závaczki Z, Szöllosi J, Koloszar S, Daru J, Kovacs L, Pal A)

Fejes I, Závaczki Z, Szöllosi J, et al. (2005) Is there a relationship between cell phone use and semen quality? Archives of Andrology 51(5):385-93.

This study was conducted to determine a possible relationship between regular cell phone use and different human semen attributes. The history-taking of men in our university clinic was supplemented with questions concerning cell phone use habits, including possession, daily standby position and daily transmission times. Semen analyses were performed by conventional methods. Statistics were calculated with SPSS statistical software. A total of 371 were included in the study. The duration of possession and the daily transmission time correlated negatively with the proportion of rapid progressive motile sperm ($r = -0.12$ and $r = -0.19$, respectively), and positively with the proportion of slow progressive motile sperm ($r = 0.12$ and $r = 0.28$, respectively). The low and high transmitter groups also differed in the proportion of rapid progressive motile sperm (48.7% vs. 40.6%). The prolonged use of cell phones may have negative effects on the sperm motility characteristics.

(Fragopoulou A, Grigoriev Y, Johansson O, Margaritis LH, Morgan L, Richter E, Sage C)

Fragopoulou A, Grigoriev Y, Johansson O, et al. (2010) Scientific Panel on Electromagnetic Field Health Risks: Consensus points, recommendations, and rationales. Reviews on Environmental Health 25(4):307-17.

In November, 2009, a scientific panel met in Seletun, Norway, for three days of intensive discussion on existing scientific evidence and public health implications of the unprecedented global exposures to artificial electromagnetic fields (EMF). EMF exposures (static to 300 GHz) result from the use of electric power and from wireless telecommunications technologies for voice and data transmission, energy, security, military and radar use in weather and transportation. The Scientific Panel recognizes that the body of evidence on EMF requires a new approach to protection of public health; the growth and development of the fetus, and of children; and argues for strong

preventative actions. New, biologically-based public exposure standards are urgently needed to protect public health worldwide.

Girgert R, Gründker C, Emons G, Hanf V (2008) Electromagnetic fields alter the expression of estrogen receptor cofactors in breast cancer cells. Bioelectromagnetics 29(3):169-76.

Breast cancer is the most common malignancy of women in Western societies. The increasing exposure to electromagnetic fields has been suspected to contribute to the rising incidence of breast cancer in industrialized countries. The majority of breast tumors is treated with the partial antiestrogen tamoxifen. Most tumors become resistant to tamoxifen in the course of treatment resulting in treatment failure. Electromagnetic fields reduce the efficacy of tamoxifen similar to tamoxifen resistance. In this study we investigated the mechanism by which electromagnetic fields influence the sensitivity to tamoxifen. In cells exposed to 1.2 microT of a 50 Hz electromagnetic field gene expression of cofactors of the estrogen receptors was compared to sham exposed cells. Using a gene array technology several cofactors were found to be differentially expressed. The expression of the coactivators, SRC-1 and AIB1, and of two corepressors, N-Cor and SMRT, was quantified by RT-PCR. Both coactivators were expressed more strongly in the exposed cells while the expression of two corepressors decreased. The RNA analysis was confirmed by Western blots. The contradirectional changes in gene expression of coactivators and corepressors by electromagnetic fields results in a lower sensitivity to tamoxifen. Electromagnetic fields may contribute to the induction of tamoxifen resistance in vivo.

**(Grigoriev YG, Grigoriev OA, Ivanov AA, Lyaginskaya AM, Merkulov AV, Shagina NB, Maltsev VN, Lévêque P, Ulanova AM, Osipov VA, Shafirkin AV.)
Grigoriev YG, Grigoriev OA, Ivanov AA, et al. (2010) Confirmation studies of Soviet research on immunological effects of microwaves: Russian immunology results. Bioelectromagnetics 31(8):589-602.**

This paper presents the results of a replication study performed to investigate earlier Soviet studies conducted between 1974 and 1991 that showed immunological and reproductive effects of long-term low-level exposure of rats to radiofrequency (RF) electromagnetic fields. The early studies were used, in part, for developing exposure standards for the USSR population and thus it was necessary to confirm the Russian findings. In the present study, the conditions of RF exposure were made as similar as possible to those in the earlier experiments: Wistar rats were exposed in the far field to 2450 MHz continuous wave RF fields with an incident power density in the cages of 5 W/m² for 7 h/day, 5 days/week for a total of 30 days, resulting in a whole-body SAR of 0.16 W/kg. Effects of the exposure on immunological parameters in the brain and liver of rats were evaluated using the complement fixation test (CFT), as in the original studies, and an additional test, the more modern ELISA test. Our results, using CFT and ELISA, partly confirmed the findings of the early studies and indicated possible effects from non-thermal RF exposure on autoimmune processes. The RF exposure resulted in minor increases in formation of antibodies in brain tissue extract and the exposure did not appear to be pathological. In addition, a study was conducted to replicate a previous Soviet study on effects from the injection of blood serum from RF-exposed rats on pregnancy and foetal and offspring development of rats, using a similar animal model and protocol. Our results showed the same general trends as the earlier study, suggesting possible adverse effects of the blood serum from exposed rats on pregnancy and foetal development of intact rats, however, application of these results in developing exposure standards is limited.

Gul A, Celebi H, Uğraş S (2009) The effects of microwave emitted by cellular phones on ovarian follicles in rats. Archives of Gynecology and Obstetrics 280(5):729-33.

OBJECTIVE: The aim of this study was to investigate whether there were any toxic effects of microwaves of cellular phones on ovaries in rats.

METHODS: In this study, 82 female pups of rats, aged 21 days (43 in the study group and 39 in the control group) were used. Pregnant rats in the study group were exposed to mobile phones that were

placed beneath the polypropylene cages during the whole period of pregnancy. The cage was free from all kinds of materials, which could affect electromagnetic fields. A mobile phone in a standby position for 11 h and 45 min was turned on to speech position for 15 min every 12 h and the battery was charged continuously. On the 21st day after the delivery, the female rat pups were killed and the right ovaries were removed. The volumes of the ovaries were measured and the number of follicles in every tenth section was counted.

RESULTS: The analysis revealed that in the study group, the number of follicles was lower than that in the control group. The decreased number of follicles in pups exposed to mobile phone microwaves suggest that intrauterine exposure has toxic effects on ovaries.

CONCLUSION: We suggest that the microwaves of mobile phones might decrease the number of follicles in rats by several known and, no doubt, countless unknown mechanisms.

Gutschi T, Mohamad Al-Ali B, Shamloul R, Pummer K, Trummer H (2011) Impact of cell phone use on men's semen parameters. *Andrologia* 43(5):312-6.

The objective of the present retrospective study was to report our experience concerning the effects of cell phone usage on semen parameters. We examined 2110 men attending our infertility clinic from 1993 to October 2007. Semen analysis was performed in all patients. Serum free testosterone (T), follicle stimulating hormone (FSH), luteinising hormone (LH) and prolactin (PRL) were collected from all patients. The information on cell phone use of the patients was recorded and the subjects were divided into two groups according to their cell phone use: group A: cell phone use (n = 991); group B: no use (n = 1119). Significant difference was observed in sperm morphology between the two groups. In the patients of group A, 68.0% of the spermatozoa featured a pathological morphology compared to only 58.1% in the subjects of group B. Patients with cell phone usage showed significantly higher T and lower LH levels than those who did not use cell phone. No significant difference between the two groups was observed regarding FSH and PRL values. Our results showed that cell phone use negatively affects sperm quality in men. Further studies with a careful design are needed to determine the effect of cell phone use on male fertility.

Hardell L, Carlberg M, Ohlson CG, Westberg H, Eriksson M, Hansson Mild K (2007) Use of cellular and cordless telephones and risk of testicular cancer. *International Journal of Andrology* 30(2):115-22.

A case-control study on testicular cancer included use of cellular and cordless telephones. The results were based on answers from 542 (92%) cases with seminoma, 346 (89%) with non-seminoma, and 870 (89%) controls. Regarding seminoma the use of analog cellular phones gave odds ratio (OR) = 1.2, 95% confidence interval (CI) = 0.9-1.6, digital phones OR = 1.3, CI = 0.9-1.8, and cordless phones OR = 1.1, CI = 0.8-1.5. The corresponding results for non-seminoma were OR = 0.7, CI = 0.5-1.1, OR = 0.9, CI = 0.6-1.4, and OR = 1.0, CI = 0.7-1.4, respectively. There was no dose-response effect and OR did not increase with latency time. No association was found with place of keeping the mobile phone during standby, such as trousers pocket. Cryptorchidism was associated both with seminoma (OR = 4.2, CI = 2.7-6.5) and non-seminoma (OR = 3.3, CI = 2.0-5.6), but no interaction was found with the use of cellular or cordless telephones.

Irgens A, Kruger K, Ulstein M. (1999) The effect of male occupational exposure in infertile couples in Norway. *Journal of Occupational and Environmental Medicine* 41(12):1116-1120.

The objective of the study was to assess whether reduced semen quality in infertile couples is associated with occupational exposures known to be hazardous to fertility. Results of the first semen analysis were linked to occupational exposure data from a self-administered questionnaire. Reduced semen quality was found in men exposed to electromagnetic fields (odds ratio, 3.22; confidence interval, 1.46 to 7.09). A tendency toward reduced semen quality was seen in commuters (OR, 1.52; CI, 0.89 to 2.59), shift workers (OR, 1.46; CI, 0.89 to 2.40), and men exposed to heavy metals (OR, 1.47; CI, 0.76 to 2.87). In general, the impact of occupational

exposure on semen quality in infertile couples in Norway seemed to be minor. However, occupational exposure mapping is still important in individual infertility investigations.

Kesari KK, Kumar S, Behari J (2011) Effects of radiofrequency electromagnetic wave exposure from cellular phones on the reproductive pattern in male Wistar rats. *Applied Biochemistry and Biotechnology* 164(4):546-59.

The present study investigates the effect of free radical formation due to mobile phone exposure and effect on fertility pattern in 70-day-old male Wistar rats (sham exposed and exposed). Exposure took place in Plexiglas cages for 2 h a day for 35 days to mobile phone frequency. The specific absorption rate was estimated to be 0.9 W/kg. An analysis of antioxidant enzymes glutathione peroxidase ($P < 0.001$) and superoxide dismutase ($P < 0.007$) showed a decrease, while an increase in catalase ($P < 0.005$) was observed. Malondialdehyde ($P < 0.003$) showed an increase and histone kinase ($P = 0.006$) showed a significant decrease in the exposed group. Micronuclei also show a significant decrease ($P < 0.002$) in the exposed group. A significant change in sperm cell cycle of G(0)-G(1) ($P = 0.042$) and G(2)/M ($P = 0.022$) were recorded. Generation of free radicals was recorded to be significantly increased ($P = 0.035$). Our findings on antioxidant, malondialdehyde, histone kinase, micronuclei, and sperm cell cycle are clear indications of an infertility pattern, initiated due to an overproduction of reactive oxygen species. It is concluded that radiofrequency electromagnetic wave from commercially available cell phones might affect the fertilizing potential of spermatozoa.

Kilgallon SJ, Simmons LW (2005) Image content influences men's semen quality. *Biology Letters* 1(3):253-5.

There is increasing evidence from non-human animals that males adjust their ejaculate expenditure according to the risk of sperm competition. In this study we show that, after controlling for lifestyle factors known to influence semen quality, human males viewing images depicting sperm competition had a higher percentage of motile sperm in their ejaculates. Many lifestyle variables were confirmed to influence semen quality, including the recent suggestion that storage of mobile phones close to the testes can decrease semen quality.

(Kim YW, Kim HS, Lee JS, Kim YJ, Lee SK, Seo JN, Jung KC, Kim N, Gimm YM.) Kim YW, Kim HS, Lee JS, et al. (2009) Effects of 60 Hz 14 microT magnetic field on the apoptosis of testicular germ cell in mice. *Bioelectromagnetics* 30(1):66-72.

We recently reported that continuous exposure, for 8 weeks, of extremely low frequency (ELF) magnetic field (MF) of 0.1 or 0.5 mT might induce testicular germ cell apoptosis in BALB/c mice. In that report, the ELF MF exposure did not significantly affect the body weight or testicular weight, but significantly increased the incidence of testicular germ cell death. In the present study, we aimed to further characterize the effect of a 16-week continuous exposure to ELF MF of 14 or 200 microT on testicular germ cell apoptosis in mice. There were no significant effects of MF on body weight and testosterone levels in mice. In TUNEL staining (In situ terminal deoxynucleotidyl transferase-mediated deoxy-UTP nick end labeling), germ cells showed a significantly higher apoptotic rate in exposed mice than in sham controls ($P < 0.001$). TUNEL-positive cells were mainly spermatogonia. In an electron microscopic study, degenerating spermatogonia showed condensation of nuclear chromatin similar to apoptosis. These results indicate that apoptosis may be induced in spermatogenic cells in mice by continuous exposure to 60 Hz MF of 14 microT.

Koldayev VM, Shchepin YV. (1997) Effects of electromagnetic radiation on embryos of sea-urchins. *Bioelectrochemistry and Bioenergetics* 43:161-164.

Electromagnetic radiation (EMR) causes a decrease in the number of fertilized eggs and an increase in the number of zygotes with abnormal fertilization envelopes in sea-urchins. The microstructural impairments of the cellular surface, the increase of lipid peroxidation and the changes of amino acid

metabolism show that the impairments of the development of embryos exposed to EMR are caused by the damages of the membrane structures.

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

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

Khurana VG, Teo C, Bittar RG. (2009) Health risks of cell phone technology. Surgical Neurology 72(4):436-7; author reply 437.

Comment on Pawl R. (2008) Cell phones more dangerous than cigarettes! Surgical Neurology 70(5):445-6.

Dear Editor:

The editorial by Dr Pawl [12] is timely and discusses an emerging public health concern. This reignited debate [9] has not escaped the attention of the US Congress, whose Subcommittee on Domestic Policy chaired by Congressman Dennis Kucinich held a landmark hearing regarding this topic on September 25, 2008 [7]. The proposed health ramifications of ubiquitous and chronic immersion in the electromagnetic fields (EMFs) of cell phones and transmission masts are not only limited to brain tumors but also include salivary gland tumors [13], male infertility [1,5], behavioral disturbances [4], and electrohypersensitivity (previously "microwave sickness syndrome") [10]. Since the publication of the seminal BioInitiative Report [2] in August 2007 by a multinational group of recognized scientists, physicians, and policy makers, important steps have been taken in many countries [8], urging evidence-based precaution as compelling new long-term epidemiologic data accrue from the Hardell group and World Health Organization-administered INTERPHONE consortium [6]. It is recommended that serial age-adjusted primary central nervous system tumor incidence rates from databases, such as those of the Central Brain Tumor Registry of the United States [3], be carefully followed in time for trends. Although there is no currently proven mechanism via which cell phone radiation can cause neoplasia, it is notable that there are more than one dozen peer-reviewed papers from laboratories in at least 7 countries including the United States showing that cell phone or similar low-intensity EMFs can break DNA or modulate it structurally [11], despite comments stating otherwise [14]. A simple precautionary step includes using a landline in preference to a cell phone whenever possible. If talking on a cell phone, a wired earpiece or speaker-phone mode should be used to increase the distance between the antenna (external or concealed) and the user's head. Restricting children's cell phone usage should also be strongly considered given the recent testimony of Dr Ronald Herberman and Dr David Carpenter [7].

January 2, 2012

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Available online at www.sciencedirect.com

Surgical Neurology xx (2009) xxx

www.surgicalneurology-online.com

0090-3019/\$ – see front matter © 2009 Published by Elsevier Inc.

doi:10.1016/j.surneu.2008.11.013

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January 2, 2012

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[14] Vogel G. Fraud charges cast doubt on claims of DNA damage from cell phone fields. *Science* 2008;321:1144-5.

Commentary

Obviously, I cannot agree with Dr Khurana more. His cautions are in line with my own, as stated in the referenced editorial. He is one of the finders; I am just a messenger. Hopefully, the committee action initiated by Congressman Kucinich will lead to appropriate further research and regulatory changes as needed.

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Larsen AI, Olsen J, Svane O. (1991) Gender-specific reproductive outcome and exposure to high-frequency electromagnetic radiation among physiotherapists. *Scandinavian Journal of Work and Environmental Health* 17(5):324-329.

The aim of this case-referent study was to investigate reproductive hazards other than congenital malformations after exposure to high-frequency electromagnetic radiation. Cases and referents were sampled from a cohort of pregnancies of members of the Union of Danish Physiotherapists through linkage of the union file with national medical registers. Case groups were spontaneous abortions and children with low birth-weight prematurity, and stillbirth/death within one year. Exposure to high-frequency electromagnetic radiation before and during pregnancy was assessed through telephone interviews. As referents to the 270 cases, 316 pregnancies were randomly sampled. A total of 8.4% did not participate. Only 23.5% of the children born by the highly exposed mothers were boys. This value is a statistically significantly altered gender ratio showing a dose-response pattern. High-frequency electromagnetic radiation was furthermore associated with low birthweight, but only for male newborns. The other outcomes were not statistically significantly associated with exposure to high-frequency electromagnetic radiation.

La Vignera S, Condorelli RA, Vicari E, D'Agata R, Calogero AE (2011) Effects of the exposure to mobile phones on male reproduction: a review of the literature. *Journal of Andrology* Jul 28. [Epub ahead of print]

The use of mobile phones is now widespread. A great debate is going on about the possible damage that the radiofrequency electromagnetic radiation (RF-EMR) emitted by mobile phones exerts on different organs and apparatuses. Aim of this article was to review the existing literature exploring the effects of RF-EMR on the male reproductive function in experimental animals and human beings. Studies on the experimental animals have been conducted in rats, mice, and rabbits using a similar design based upon mobile phone radiofrequency exposure for a variable length of time. Altogether the results of these studies show that RF-EMR decreases sperm count and motility, and increases the oxidative stress. In human beings, two different experimental approaches have been followed, one has explored the effects of RF-EMR directly on spermatozoa and the other has evaluated the sperm parameters in men using or not mobile phones. The results show that human spermatozoa exposed to RF-EMR have decreased motility, morphometric abnormalities, and increased oxidative stress, whereas men using mobile phones have decreased sperm concentration, motility (particularly the rapid progressive one), normal morphology, and viability. These abnormalities seem to be directly related with the length of mobile phone use.

Lee GM, Neutra RR, Hristova L, Yost M, Hiatt RA (2002) A nested case-control study of residential and personal magnetic field measures and miscarriages. *Epidemiology* 13(1):21-31. Erratum in *Epidemiology* 2003 4(2):255.

January 2, 2012

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We conducted a nested case-control study (177 cases, 550 controls) to assess the relation between retrospective magnetic field measures and clinical miscarriage among members of the northern California Kaiser Permanente medical care system. We also conducted a prospective substudy of 219 participants of the same parent cohort to determine whether 12-week and 30-week exposure assessments were similar. We evaluated wire codes, area measures, and three personal meter metrics: (1) the average difference between consecutive levels (a rate-of-change metric), (2) the maximum level, and (3) the time-weighted average. For wire codes and area measures we found little association. For the personal metrics (30 weeks after last menstrual period), we found positive associations. Each exposure was divided into quartiles, with the lowest quartile as referent. Starting with the highest quartile, adjusted odds ratios and 95% confidence intervals were 3.1 (95% CI = 1.6-6.0), 2.3 (95% CI = 1.2-4.4), and 1.5 (95% CI = 0.8-3.1) for the rate-of-change metric; 2.3 (95% CI = 1.2-4.4), 1.9 (95% CI = 1.0-3.5), and 1.4 (95% CI = 0.7-2.8) for the maximum value; and 1.7 (95% CI = 0.9-3.3), 1.7 (95% CI = 0.9-3.3), and 1.7 (95% CI = 0.9-3.3) for the time-weighted average. The odds ratio conveyed by being above a 24-hour time-weighted average of 2 milligauss was 1.0 (95% CI = 0.5-2.1). Exposure assessment measurements at 12 weeks were poorly correlated with those taken at 30 weeks. Nonetheless, the prospective substudy results regarding miscarriage risk were consistent with the nested study results.

Comment in

- Epidemiology. 2002 Jan;13(1):1-4.
- Epidemiology. 2002 Mar;13(2):237-8.
- Epidemiology. 2002 May;13(3):372.

Lee JW, Kim KS, Lee SM, Eom SJ, Troitsky RV (2002) A novel design of thermal anomaly for mammary gland tumor phantom for microwave radiometer. IEEE Transactions on Bio-medical Engineering 49(7):694-9.

Microwave radiometry is the spectral measurement technique of resolving electromagnetic radiation of all matters which temperature is above absolute zero. This technique utilizes the electromagnetic noise field generated by a thermal volume similar to a mechanism existing in biological tissues. One particular application of microwave radiometry is for analyzing temperature differentials of inside of human body to detect and diagnose some crucial pathological conditions. For the general evaluation of a microwave radiometer, we propose a new type of phantom containing a mammary gland tumor imitator by considering biological heat diffusion effects propagated by a real tumor. Theoretical researches of human tumor revealed the fact that temperature distribution of tissues around a tumor formed a Gaussian statistics. To comply with the physiological property of the real tumor, we built a mammary gland tumor imitator composed of two parts (pseudotumor and thermal anomaly) and observed its temperature distribution when it was placed inside a phantom. Our results showed that the thermal properties of tumor imitator well agreed with heat-transfer properties of a real tumor and the proportional linear relationship existed between the location of tumor imitator and the intensity of radiometer measurements. From this relationship, we could also estimate several parameters related with our phantom, such as the minimum detectable size and maximum detectable depth of a tumor imitator.

Li DK, Yan B, Li Z, Gao E, Miao M, Gong D, Weng X, Ferber JR, Yuan W (2010) Exposure to magnetic fields and the risk of poor sperm quality. Reproductive Toxicology 29(1):86-92.

We conducted a population-based case-control study among healthy sperm donors to study exposure to magnetic fields (MFs) and poor sperm quality. All participants wore a meter to capture daily MF exposure. After controlling for confounders, compared to those with lower MF exposure, those whose 90th percentile MF level ≥ 1.6 mG had a two-fold increased risk of abnormal sperm motility and morphology (odds ratio (OR): 2.0, 95% confidence interval (CI): 1.0-3.9). Increasing duration of MF exposure above 1.6 mG further increased the risk ($p=0.03$ for trend test). Importantly, the association and dose-response relationship were strengthened when restricted to those whose measurement day reflected their typical day of the previous 3 months (a likely period of spermatogenesis). Age-adjusted Spearman Rank Order Correlations showed an inverse

correlation between MF exposure and all semen parameters. Our study provides some evidence for the first time that MF exposure may have an adverse effect on sperm quality.

Magras IN, Xenos TD (1997) RF radiation-induced changes in the prenatal development of mice. Bioelectromagnetics 18(6):455-61.

The possible effects of radiofrequency (RF) radiation on prenatal development has been investigated in mice. This study consisted of RF level measurements and in vivo experiments at several places around an "antenna park." At these locations RF power densities between 168 nW/cm² and 1053 nW/cm² were measured. Twelve pairs of mice, divided in two groups, were placed in locations of different power densities and were repeatedly mated five times. One hundred eighteen newborns were collected. They were measured, weighed, and examined macro- and microscopically. A progressive decrease in the number of newborns per dam was observed, which ended in irreversible infertility. The prenatal development of the newborns, however, evaluated by the crown-rump length, the body weight, and the number of the lumbar, sacral, and coccygeal vertebrae, was improved.

Mailankot M, Kunnath AP, Jayalekshmi H, Koduru B, Valsalan R. Radio frequency electromagnetic radiation (RF-EMR) from GSM (0.9/1.8GHz) mobile phones induces oxidative stress and reduces sperm motility in rats. Clinics (Sao Paulo). 2009;64(6):561-5.

INTRODUCTION: Mobile phones have become indispensable in the daily lives of men and women around the globe. As cell phone use has become more widespread, concerns have mounted regarding the potentially harmful effects of RF-EMR from these devices.

OBJECTIVE: The present study was designed to evaluate the effects of RF-EMR from mobile phones on free radical metabolism and sperm quality.

MATERIALS AND METHODS: Male albino Wistar rats (10-12 weeks old) were exposed to RF-EMR from an active GSM (0.9/1.8 GHz) mobile phone for 1 hour continuously per day for 28 days. Controls were exposed to a mobile phone without a battery for the same period. The phone was kept in a cage with a wooden bottom in order to address concerns that the effects of exposure to the phone could be due to heat emitted by the phone rather than to RF-EMR alone. Animals were sacrificed 24 hours after the last exposure and tissues of interest were harvested.

RESULTS: One hour of exposure to the phone did not significantly change facial temperature in either group of rats. No significant difference was observed in total sperm count between controls and RF-EMR exposed groups. However, rats exposed to RF-EMR exhibited a significantly reduced percentage of motile sperm. Moreover, RF-EMR exposure resulted in a significant increase in lipid peroxidation and low GSH content in the testis and epididymis.

CONCLUSION: Given the results of the present study, we speculate that RF-EMR from mobile phones negatively affects semen quality and may impair male fertility.

Makker K, Varghese A, Desai NR, Mouradi R, Agarwal A. (2009) Cell phones: modern man's nemesis? Reprod Biomed Online. 2009 Jan;18(1):148-57.

Over the past decade, the use of mobile phones has increased significantly. However, with every technological development comes some element of health concern, and cell phones are no exception. Recently, various studies have highlighted the negative effects of cell phone exposure on human health, and concerns about possible hazards related to cell phone exposure have been growing. This is a comprehensive, up-to-the-minute overview of the effects of cell phone exposure on human health. The types of cell phones and cell phone technologies currently used in the world are discussed in an attempt to improve the understanding of the technical aspects, including the effect of cell phone exposure on the cardiovascular system, sleep and cognitive function, as well as localized and general adverse effects, genotoxicity potential, neurohormonal secretion and tumour induction. The proposed mechanisms by which cell phones adversely affect various aspects of human health, and male fertility in particular, are explained, and the emerging molecular techniques

and approaches for elucidating the effects of mobile phone radiation on cellular physiology using high-throughput screening techniques, such as metabolomics and microarrays, are discussed. A novel study is described, which is looking at changes in semen parameters, oxidative stress markers and sperm DNA damage in semen samples exposed in vitro to cell phone radiation.

Moskowitz JM (2011) Research on the effects of cell phone radiation on human sperm.

CEAC. Available at:

http://www.ci.berkeley.ca.us/uploadedFiles/Planning_and_Development/Level_3_-_Commissions/Commission_for_Community_Environmental_Advisory/CEAC2011-04-07_1i-Effects_of_CellPhoneRadiation_onHumanSperm-Moskowitz.pdf

The following terms were used in a PubMed search: (cell or mobile) phone sperm. Fourteen English-language, papers were found that examined the effects of cell phone radiation on human sperm including nine original studies and five review papers. Eight of the nine original studies reported adverse effects of cell phone radiation on at least one of four outcomes: sperm count (C), motility (M), viability (V) or morphology (S). The adverse effects obtained in these studies were as follows: C/M/V/S (Agarwal et al., 2008a); M/V (Agarwal et al., 2009; De luliis et al., 2009); M/S (Wdowiak et al., 2007); M (Erogul et al., 2006; Fejes et al., 2005); and S (Falzone et al., 2008; Falzone et al., 2011). The ninth study examined sperm for signs of pre-apoptosis but found no evidence for this mechanism (Falzone et al., 2010). Cell phone radiation was associated with decreased sperm motility (M) in six of the eight studies that assessed this outcome. The next most commonly observed effect was reduced viability (V) in three studies. Note that not all studies measured each of these four outcomes. The research abstracts from the search follow. The original studies are in the first section followed by the review papers. The abstracts are listed in alphabetical order by first author.

Nakamura H, Nagase H, Ogino K, Hatta K, Matsuzaki I. (2000) Uteroplacental circulatory disturbance mediated by prostaglandin F(2alpha) in rats exposed to microwaves. Reproductive Toxicology 14(3):235-240.

To clarify the effects of microwaves on pregnancy, uterine or uteroplacental blood flow and endocrine and biochemical mediators, including corticosterone, estradiol, prostaglandin E(2) (PGE(2)), and prostaglandin F(2)alpha (PGF(2)alpha), were measured in rats exposed to continuous-wave (CW) microwave at 2 mW/cm(2) incident power density at 2450 MHz for 90 min. Colonic temperature in virgin and pregnant rats was not significantly altered by microwave treatment. Microwaves decreased uteroplacental blood flow and increased progesterone and PGF(2)alpha in pregnant, but not in virgin rats. Intraperitoneal (i.p.) administration of angiotensin II, a uteroplacental vasodilator, before microwave exposure prevented the reduction in uteroplacental blood flow and the increased progesterone and PGF(2)alpha in pregnant rats. Increased corticosterone and decreased estradiol during microwave exposure were observed independent of pregnancy and pretreatment with angiotensin II. These results suggest that microwaves (CW, 2 mW/cm(2), 2450 MHz) produce uteroplacental circulatory disturbances and ovarian and placental dysfunction during pregnancy, probably through nonthermal actions. The uteroplacental disturbances appear to be due to actions of PGF(2)alpha and may pose some risk for pregnancy.

Otitoloju AA, Obe IA, Adewale OA, Otubanjo OA, Osunkalu VO (2010) Preliminary study on the induction of sperm head abnormalities in mice, *Mus musculus*, exposed to radiofrequency radiations from global system for mobile communication base stations. Bulletin of Environmental Contamination and Toxicology 84(1):51-4.

The exposure of male mice to radiofrequency radiations from mobile phone (GSM) base stations at a workplace complex and residential quarters caused 39.78 and 46.03%, respectively, in sperm head abnormalities compared to 2.13% in control group. Statistical analysis of sperm head abnormality score showed that there was a significant ($p < 0.05$) difference in occurrence of sperm head abnormalities in test animals. The major abnormalities observed were knobbed hook, pin-head and

banana-shaped sperm head. The occurrence of the sperm head abnormalities was also found to be dose dependent. The implications of the observed increase occurrence of sperm head abnormalities on the reproductive health of humans living in close proximity to GSM base stations were discussed.

Panagopoulos DJ, Karabarbounis A, Margaritis LH (2004) Effect of GSM 900-MHz mobile phone radiation on the reproductive capacity of *Drosophila melanogaster* Electromagnetic biology and medicine 23:29-43.

Pulsed radio frequency, (RF), electromagnetic radiation from common GSM mobile phones, (Global System for Mobile Telecommunications) with a carrier frequency at 900 MHz, “modulated” by human voice, (speaking emission) decreases the reproductive capacity of the insect *Drosophila melanogaster* by 50%–60%, whereas the corresponding “nonmodulated” field (nonspeaking emission) decreases the reproductive capacity by 15%–20%. The insects were exposed to the near field of the mobile phone antenna for 6 min per day during the first 2–5 days of their adult lives. The GSM field is found to affect both females and males. Our results suggest that this field-radiation decreases the rate of cellular processes during gonad development in insects.

Panagopoulos DJ, Margaritis LH (2008) Mobile telephony radiation effects on living organisms. In: Harper AC, Buress RV, eds. Mobile Telephones. Nova Science Publishers, Inc: 107-49.

A number of serious non thermal biological effects, ranging from changes in cellular function like proliferation rate changes or gene expression changes to cell death induction, decrease in the rate of melatonin production and changes in electroencephalogram patterns in humans, population declinations of birds and insects, and small but statistically significant increases of certain types of cancer, are attributed in our days to the radiations emitted by mobile telephony antennas of both handsets and base stations. This chapter reviews briefly the most important experimental, clinical and statistical findings and presents more extensively a series of experiments, concerning cell death induction on a model biological system. Mobile telephony radiation is found to decrease significantly and non-thermally insect reproduction by up to 60%, after a few minutes daily exposure for only few days. Both sexes were found to be affected. The effect is due to DNA fragmentation in the gonads caused by both types of digital mobile telephony radiation used in Europe, GSM 900MHz, (Global System for Mobile telecommunications), and DCS 1800MHz, (Digital Cellular System). GSM was found to be even more bioactive than DCS, due to its higher intensity under equal conditions. The decrease in reproductive capacity seems to be non-linearly depended on radiation intensity, exhibiting a peak for intensities higher than 200 $\mu\text{W}/\text{cm}^2$ and an intensity “window” around 10 $\mu\text{W}/\text{cm}^2$ where it becomes maximum. In terms of the distance from a mobile phone antenna, the intensity of this “window” corresponds under usual conditions to a distance of 20-30 cm. The importance of different parameters of the radiation like intensity, carrier frequency and pulse repetition frequency, in relation to the recorded effects are discussed. Finally, this chapter describes a plausible biophysical and biochemical mechanism which can explain the recorded effects of mobile telephony radiations on living organisms.

Peyman A, Khalid M, Calderon C, Addison D, Mee T, Maslanyj M, Mann S. (2011) Assessment of exposure to electromagnetic fields from wireless computer networks (wi-fi) in schools; results of laboratory measurements. Health Phys. 100(6):594-612.

Laboratory measurements have been carried out with examples of Wi-Fi devices used in UK schools to evaluate the radiofrequency power densities around them and the total emitted powers. Unlike previous studies, a 20 MHz bandwidth signal analyzer was used, enabling the whole Wi-Fi signal to be captured and monitored. The radiation patterns of the laptops had certain similarities, including a minimum toward the torso of the user and two maxima symmetrically opposed across a vertical plane bisecting the screen and keyboard. The maxima would have resulted from separate antennas mounted behind the top left and right corners of the laptop screens. The patterns for access points were more symmetrical with generally higher power densities at a given distance. The

spherically-integrated radiated power (IRP) ranged from 5 to 17 mW for 15 laptops in the 2.45 GHz band and from 1 to 16 mW for eight laptops in the 5 GHz band. For practical reasons and because access points are generally wall-mounted with beams directed into the rooms, their powers were integrated over a hemisphere. These ranged from 3 to 28 mW for 12 access points at 2.4 GHz and from 3 to 29 mW for six access points at 5 GHz. In addition to the spherical measurements of IRP, power densities were measured at distances of 0.5 m and greater from the devices, and consistent with the low radiated powers, these were all much lower than the ICNIRP reference level.

Pyrpasopoulou A, Kotoula V, Cheva A, Hytiroglou P, Nikolakaki E, Magras IN, Xenos TD, Tsiboukis TD, Karkavelas G. (2004) Bone morphogenetic protein expression in newborn rat kidneys after prenatal exposure to radiofrequency radiation. *Bioelectromagnetics* 25(3):216-227.

Effects of nonthermal radiofrequency radiation (RFR) of the global system of mobile communication (GSM) cellular phones have been as yet mostly studied at the molecular level in the context of cellular stress and proliferation, as well as neurotransmitter production and localization. In this study, a simulation model was designed for the exposure of pregnant rats to pulsed GSM-like RFR (9.4 GHz), based on the different resonant frequencies of man and rat. The power density applied was 5 microW/cm², in order to avoid thermal electromagnetic effects as much as possible. Pregnant rats were exposed to RFR during days 1-3 postcoitum (p.c.) (embryogenesis, pre-implantation) and days 4-7 p.c. (early organogenesis, peri-implantation). Relative expression and localization of bone morphogenetic proteins (BMP) and their receptors (BMPR), members of a molecular family currently considered as major endocrine and autocrine morphogens and known to be involved in renal development, were investigated in newborn kidneys from RFR exposed and sham irradiated (control) rats. Semi-quantitative duplex RT-PCR for BMP-4, -7, BMPR-IA, -IB, and -II showed increased BMP-4 and BMPR-IA, and decreased BMPR-II relative expression in newborn kidneys. These changes were statistically significant for BMP-4, BMPR-IA, and -II after exposure on days 1-3 p.c. ($P < .001$ each), and for BMP-4 and BMPR-IA after exposure on days 4-7 p.c. ($P < .001$ and $P = .005$, respectively). Immunohistochemistry and in situ hybridization (ISH) showed aberrant expression and localization of these molecules at the histological level. Our findings suggest that GSM-like RFR interferes with gene expression during early gestation and results in aberrations of BMP expression in the newborn. These molecular changes do not appear to affect renal organogenesis and may reflect a delay in the development of this organ. The differences of relative BMP expression after different time periods of exposure indicate the importance of timing for GSM-like RFR effects on embryonic development.

Redmayne M, Smith E, Abramson MJ (2011) Adolescent in-school cellphone habits: a census of rules, survey of their effectiveness, and fertility implications. *Reproductive Toxicology* 32:354-9.

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

Sage C, Johansson O, Sage SA (2007) Personal digital assistant (PDA) cell phone units produce elevated extremely-low frequency electromagnetic field emissions. *Bioelectromagnetics* 28(5):386-92.

Initial tests indicate that personal and occupational use of personal digital assistants (PDAs or palm-held wireless units) produce high intensity bursts of extremely-low frequency electromagnetic fields (ELF-EMF). These emissions could result in comparatively high ELF-EMF exposure in persons that carry a PDA close to the body (i.e., in a pocket or on a belt); or held to the head for cell phone conversations. ELF-EMF emissions of 10 microT were recorded on PDAs during normal office use over a 24 h test period. Results of ELF-EMF measurements show that email transmit and receive functions produce rapid, short-duration ELF-EMF spikes in the 2-10 microT range, each lasting several seconds to over a minute apparently depending on file download size. Some units produced spikes as high as 30-60 microT during email activities. Cell phone activity on PDAs produced continuously elevated ELF-EMF readings in the 0.5-1 microT range, as opposed to the rapid spiking pattern for email receipt and transmission. Switching the PDA unit from "OFF" to "ON" position resulted in single ELF-EMF pulses of over 90 microT on two units. Email downloads into the PDA can occur randomly throughout the day and night when the unit is "ON"; thus the user who wears the PDA may be receiving high-intensity ELF-EMF pulses throughout the day and night. The frequency of email traffic on the PDA, and the power switching unit (battery unit) may affect the frequency and intensity of ELF-EMF emissions.

Salama N, Kishimoto T, Kanayama HO (2010) Effects of exposure to a mobile phone on testicular function and structure in adult rabbit. International Journal of Andrology 33(1):88-94. Comment in: International Journal of Andrology 33(1):95; author reply 96-7.

The accumulating effects of exposure to electromagnetic radiation emitted by a conventional mobile phone (standby position) on the testicular function and structure are not yet fully investigated. To study these effects longitudinally, a total of 24 adult male rabbits were randomly and equally divided into three groups. Rabbits in the first (phone) group were exposed, in specially designed cages, to radio frequency emitted from the mobile phone (800 MHz) in a standby position opposite to that of testes for 8 h daily for 12 weeks. The second group consisted of the stress controls which were kept in the same kind of cages to appreciate any cage-induced anxiety. The third group included the ordinary controls which were kept in the conventional roomy cages. Semen analysis and sperm function tests (viability, hypo-osmotic swelling and acridine orange) were conducted weekly. Histological testicular sections and serum total testosterone were also evaluated. A drop in the sperm concentration appeared in the phone group at week 6. This became statistically significant at week 8, compared with the two control (stress and ordinary) groups (133, 339 and 356 x 10⁶/mL, respectively) and to the initial sperm count (341 x 10⁶/mL) of this group. Motile sperm population showed similarity amongst the three study groups until week 10 when it declined significantly, and thereafter in the phone and stress control groups, with more significant decline in the phone animals (50, 61 and 72.4%, respectively). Histological examination showed also a significant decrease in the diameter of seminiferous tubules in the phone group vs. the stress and ordinary controls (191 microm vs. 206 and 226 microm, respectively). The other study points did not show any difference. In conclusion, low intensity pulsed radio frequency emitted by a conventional mobile phone kept in the standby position could affect the testicular function and structure in the adult rabbit.

Sheynkin Y, Jung M, Yoo P, Schulsinger D, Komaroff E (2005) Increase in scrotal temperature in laptop computer users. Human Reproduction 20(2):452-5.

BACKGROUND: Scrotal hyperthermia has been identified as a risk factor for male infertility. Laptop computers (LC) have become part of a contemporary lifestyle and have gained popularity among the younger population of reproductive age. LC are known to reach high internal operating temperatures. We evaluated the thermal effect of LC on the scrotum.

METHODS: Right and left scrotal temperature (ScT) was measured in 29 healthy volunteers in two separate 60 min sessions. ScT was recorded from thermocouples on a digital datalogger every 3 min with the working LC in a laptop position and in the same sitting position with approximated thighs without LC.

RESULTS: ScT increased significantly on the right and left side in the group with working LC (2.8

degrees C and 2.6 degrees C, respectively; $P < 0.0001$) and without LC (2.1 degrees C, $P < 0.0001$). However, ScT elevation with working LC was significantly higher ($P < 0.0001$).

CONCLUSIONS: Working LC in a laptop position causes significant ScT elevation as a result of heat exposure and posture-related effects. Long-term exposure to LC-related repetitive transient scrotal hyperthermia is a modern lifestyle feature that may have a negative impact upon spermatogenesis, specifically in teenage boys and young men. Further studies of such thermal effects on male reproductive health are warranted.

Sommer AM, Grote K, Reinhardt T, Streckert J, Hansen V, Lerchl A (2009) Effects of radiofrequency electromagnetic fields (UMTS) on reproduction and development of mice: a multi-generation study. Radiation Research 171(1):89-95.

Male and female mice (C57BL) were chronically exposed (life-long, 24 h/day) to mobile phone communication electromagnetic fields at approximately 1966 MHz (UMTS). Their development and fertility were monitored over four generations by investigating histological, physiological, reproductive and behavioral functions. The mean whole-body SARs, calculated for adult animals at the time of mating, were 0 (sham), 0.08, 0.4 and 1.3 W/kg. Power densities were kept constant for each group (0, 1.35, 6.8 and 22 W/m²), resulting in varying SARs due to the different numbers of adults and pups over the course of the experiment. The experiment was done in a blind fashion. The results show no harmful effects of exposure on the fertility and development of the animals. The number and the development of pups were not affected by exposure. Some data, albeit without a clear dose-response relationship, indicate effects of exposure on food consumption that is in accordance with some data published previously. In summary, the results of this study do not indicate harmful effects of long-term exposure of mice to UMTS over several generations.

Stefanis P, Drakeley A, Gazvani R, Lewis-Jones Di (2006) Growing concern over the safety of using mobile phones and male fertility. Archives of Andrology 52(1):9-14

There are growing concerns about the possible hazards of electromagnetic waves emitted by mobile phones on human health. One of the biggest concerns is their possible association with increased risk of cancer and their possible effects on cellular DNA. Electromagnetic waves can inflict their results through both thermal and non-thermal effects. There are many animal studies that show that electromagnetic waves have a wide range of damaging effects on the male reproductive system and sperm parameters. However, similar studies are quite limited in humans, and the results of animal studies should be interpreted with caution when considering their application to humans. Large controlled studies are required before confirming such possible effects on male fertility.

Tuan Anh Vu; Uyen Dinh Nguyen. (2010) Evaluation of human testis absorption in the near field of cellular phone. Communications and Electronics (ICCE), Third International Conference on

Due to the recent explosion of users in the area of mobile communications and, conveniently, most users place the cellular phone in the trouser's pocket. In this paper, a cellular phone antenna is placed close proximity to the trouser's pocket. Using FDTD (Finite Difference Time Domain) method and the male Visible Human model, the SAR (Specific Absorption Rate) distribution is calculated for the male testis. In addition, an attempt is made to simulate the reduction of SAR absorption by using simple grid metal covering the antenna.

Vu TA, Nguyen UD (2010) Evaluation of human testis absorption in the near field of cellular phone. IEEE. conference paper. DOI:10.1109/ICCE.2010.5670642

Due to the recent explosion of users in the area of mobile communications and, conveniently, most users place the cellular phone in the trouser's pocket. In this paper, a cellular phone antenna is placed close proximity to the trouser's pocket. Using FDTD (Finite Difference Time Domain)

method and the male Visible Human model, the SAR (Specific Absorption Rate) distribution is calculated for the male testis. In addition, an attempt is made to simulate the reduction of SAR absorption by using simple grid metal covering the antenna.

Wdowiak A, Wdowiak L, Wiktor H (2007) Evaluation of the effect of using mobile phones on male fertility. *Annals of Agricultural and Environmental Medicine: AAEM* 14(1):169-72.

The problem of the lack of offspring is a phenomenon concerning approximately 15% of married couples in Poland. Infertility is defined as inability to conceive after a year of sexual intercourse without the use of contraceptives. In half of the cases the causative factor is the male. Males are exposed to the effect of various environmental factors, which may decrease their reproductive capabilities. A decrease in male fertility is a phenomenon which occurs within years, which may suggest that one of the reasons for the decrease in semen parameters is the effect of the development of techniques in the surrounding environment. A hazardous effect on male fertility may be manifested by a decrease in the amount of sperm cells, disorders in their mobility, as well as structure. The causative agents may be chemical substances, ionizing radiation, stress, as well as electromagnetic waves. The objective of the study was the determination of the effect of the usage of cellular phones on the fertility of males subjected to marital infertility therapy. The following groups were selected from among 304 males covered by the study: Group A: 99 patients who did not use mobile phones, Group B: 157 males who have used GSM equipment sporadically for the period of 1-2 years, and Group C: 48 people who have been regularly using mobile phone for more than 2 years. In the analysis of the effect of GSM equipment on the semen it was noted that an increase in the percentage of sperm cells of abnormal morphology is associated with the duration of exposure to the waves emitted by the GSM phone. It was also confirmed that a decrease in the percentage of sperm cells in vital progressing motility in the semen is correlated with the frequency of using mobile phones.

Weisbrot D, Lin H, Ye L, Blank M, Goodman R. (2003) Effects of mobile phone radiation on reproduction and development in *Drosophila melanogaster*. *Journal of Cell Biochemistry* 89(1):48-55.

In this report we examined the effects of a discontinuous radio frequency (RF) signal produced by a GSM multiband mobile phone (900/1,900 MHz; SAR approximately 1.4W/kg) on *Drosophila melanogaster*, during the 10-day developmental period from egg laying through pupation. As found earlier with low frequency exposures, the non-thermal radiation from the GSM mobile phone increased numbers of offspring, elevated hsp70 levels, increased serum response element (SRE) DNA-binding and induced the phosphorylation of the nuclear transcription factor, ELK-1. The rapid induction of hsp70 within minutes, by a non-thermal stress, together with identified components of signal transduction pathways, provide sensitive and reliable biomarkers that could serve as the basis for realistic mobile phone safety guidelines.

Weyandt, TB, Schrader, SM, Turner, TW, Simon, SD. (1996) Semen analysis of military personnel associated with military duty assignments. *Reproductive Toxicology* 10(6):521-528.

A collaborative study between the U.S. Army Biomedical Research and Development Laboratory (USABRDL) and the National Institute for Occupational Safety and Health (NIOSH) was designed to assess fecundity of male artillery soldiers with potential exposures to airborne lead aerosols. Potential exposure assessment was based upon information provided in an interactive questionnaire. It became apparent from extensive questionnaire data that many soldiers in the initial control population had potentially experienced microwave exposure as radar equipment operators. As a result, a third group of soldiers without potential for lead or microwave exposures, but with similar environmental conditions, was selected as a comparison population. Blood hormone levels and semen analyses were conducted on artillerymen (n = 30), radar equipment operators (n = 20), and the comparison group (n = 31). Analysis of the questionnaire information revealed that concern about fertility problems motivated participation of some soldiers with potential artillery or

microwave exposures. Although small study population size and the confounding variable of perceived infertility limit the reliability of the study, several statistically significant findings were identified. Artillerymen who perceived a possible fertility concern demonstrated lower sperm counts/ejaculate ($P = 0.067$) and lower sperm/mL ($P = 0.014$) than the comparison group. The group of men with potential microwave exposures demonstrated lower sperm counts/mL ($P = 0.009$) and sperm/ejaculate ($P = 0.027$) than the comparison group. Variables used to assess endocrine, accessory sex gland, and sperm cell function were not different than the comparison group. Additional studies, incorporating larger numbers of individuals, should be performed in order to more optimally characterize potential lead and microwave exposure effects on male fecundity.

Yan JG, Agresti M, Bruce T, Yan YH, Granlund A, Matloub HS (2007) Effects of cellular phone emissions on sperm motility in rats. *Fertility and Sterility* 88(4):957-64.

OBJECTIVE: To evaluate the effects of cellular phone emissions on rat sperm cells.

DESIGN: Classic experimental.

SETTING: Animal research laboratory.

SUBJECTS: Sixteen 3-month-old male Sprague-Dawley rats, weighing 250-300 g.

INTERVENTION(S): Rats in the experimental group were exposed to two 3-hour periods of daily cellular phone emissions for 18 weeks; sperm samples were then collected for evaluation.

MAIN OUTCOME MEASURE(S): Evaluation of sperm motility, sperm cell morphology, total sperm cell number, and mRNA levels for two cell surface adhesion proteins.

RESULT(S): Rats exposed to 6 hours of daily cellular phone emissions for 18 weeks exhibited a significantly higher incidence of sperm cell death than control group rats through chi-squared analysis. In addition, abnormal clumping of sperm cells was present in rats exposed to cellular phone emissions and was not present in control group rats.

CONCLUSION(S): These results suggest that carrying cell phones near reproductive organs could negatively affect male fertility.

Yoshida Y, Seto T, Ohsu W, Hayashi S, Okazawa T, Nagase H, Yoshida M, Nakamura H (1995) [Endocrine mechanism of placental circulatory disturbances induced by microwave in pregnant rats]. *Nippon Sanka Fujinka Gakkai Zasshi* 47(2):101-108. [Article in Japanese]

Effects of microwaves on fetus and female genital organs remain to be elucidated. To demonstrate the placental circulatory disturbances induced by microwaves and to clarify the endocrine pathogenesis, placental blood flow and five endocrine indicators, i.e., corticosterone (CS), estradiol (E2), progesterone (P), prostaglandin E2 (PGE2) and prostaglandin F2 alpha (PGF2 alpha) were measured in rats exposed to whole-body microwaves with an intensity of 10 mW/cm² at a frequency of 2,450 MHz. The placental blood flow at 45-90 min after exposure was significantly decreased in the rats exposed to the microwaves. Placental blood flow at 15 and 30 min was increased by pretreatment with intraperitoneal administration of angiotensin II (AII). In contrast, no significant change in placental blood flow was recognized in the AII pretreated rats exposed to the microwaves. An increase in CS and a decrease in E2 were induced by the microwave exposure independent of pretreatment with AII. P was increased by microwave exposure in the rats without pretreatment with AII. PGE2 was not changed by the microwave exposure in the case of either nonpretreatment or pretreatment with AII. PGF2 alpha was increased by the microwave exposure in the rats without pretreatment with AII. The present results indicate that excessive exposure to whole-body microwave disorders pregnancy in terms of placental circulatory dysfunction. The data suggest the involvement of endocrine mechanisms in the decrease in placental blood flow which is

induced via a detrimental effect of microwaves on PGF2 alpha and on pituitary functions such as general emotional stress.

Youbicier-Simo, BJ, Lebecq, JC, Bastide, M. (1998) Mortality of chicken embryos exposed to EMFs from mobile phones. Presented at the Twentieth Annual Meeting of the Bioelectromagnetics Society, St. Pete Beach, FL, June 1998. Exposure to mobile phone-radiated EMFs during development worsens embryonic mortality in chicken.

Conclusion: Exposure to mobile phone-radiated EMFs during development worsens embryonic mortality in chickens.

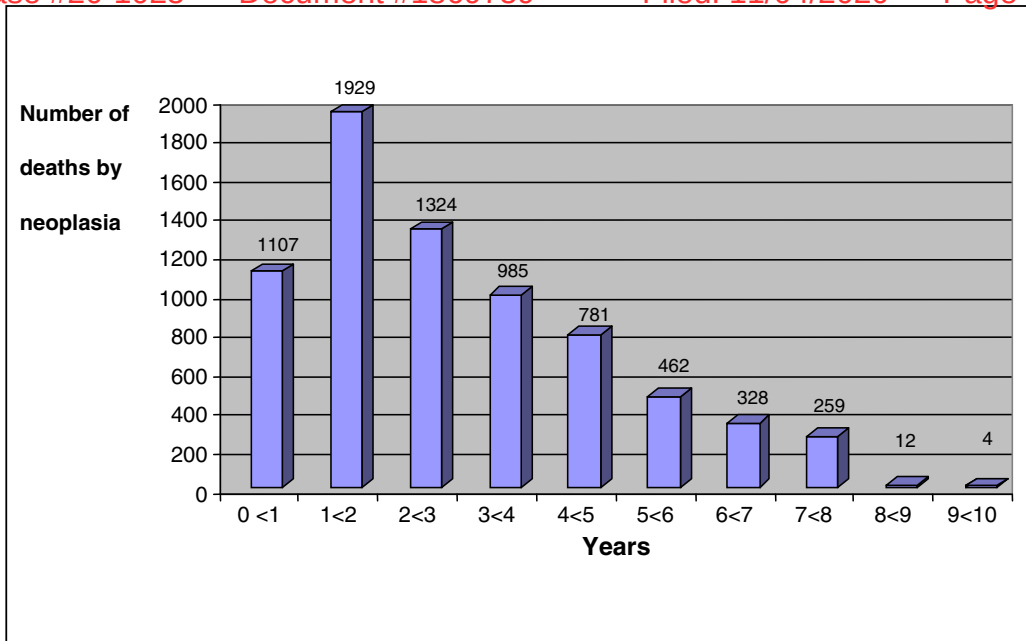
Method: We previously reported that continuous exposure of chicken embryos to electromagnetic fields (EMFs) emitted by television and computer worsens embryonic death (Bioelectromagnetics, 1997, 18: 514-523). The present study was designed to assess the effects of EMFs radiated by mobile phones on the development of chicken embryos. Two groups of 60 eggs each were incubated (21 days, $38 \pm 1^\circ\text{C}$, 45-55% humidity, permanent darkness) under the following electromagnetic exposure conditions: control group (without the telephone); exposed group (24h/24h exposure with the telephone switched on and placed downwards, 10 mm above the eggs; the letter were distributed on a plateform with locations numbered from 1 to 60; see exposure system in page 2). The mobile phone used (Bosch, CARTEL SL 2G2, Germany) radiates in the radiofrequency band with 2 W power. The VLF and ELF values measured at different positions at the level of the eggs are outlined as ratios, adjacent to the exposure system (page 2). The values over and under the bar correspond to the telephone switched off and on respectively. Embryonic mortality was evaluated by candling the eggs and numbering dead embryos at two-day intervals from embryonic day 3 (ED3) to embryonic day 13 (ED13): ED3, ED5, ED7, ED9, ED11, ED13. Counting could not be performed from ED14 to hatching (ED21) because the eggs had become so opaque (intense vascularization, increased embryo body size) that the embryos could hardly be mirrored through the shell. For the latter period, embryonic mortality was assessed by opening the eggs from which the chicks did not hatch at ED21. Three independent experiments were carried out. Embryonic mortality was expressed either as cumulative mortality (previous + current counts) or as total death rate (percentage of necropsied embryos from ED3 to ED21). In the exposed group, EMF exposure was accompanied by increased embryonic loss during the whole embryonic period, while noticeable variations in the control group occurred mainly at the end of incubation (ED21); furthermore mean total death rate (TDR) for the three experiments was 6-fold higher in EMF-exposed group than in their control counterparts (72.3% vs. 11.9%; see Table 1). Consistently, necropsy distribution in the exposed group was essentially restricted to an area around the source of EMF (mobile phone), which contrast with rather sparse distribution in the control group (see the diagrams of cumulative mortality in page 2). Together these findings demonstrate that exposure to mobile phones-radiated EMFs during development worsens embryonic mortality. [Note that this experiment was funded by the company which made the protection-antenna being tested. SF.]

<http://www.electric-words.com/cell/abstracts/yo13240.html>

Note: For seven or more, the names and initials of the first three should be given, followed by et al. All names appear here for future work and then repeated the first three et al. for this journal.

Fertility; Effects of Microwave RF Exposure on
Fertility, Dr. Paul Dart MD. (Petitioner); 2013

Belo Horizonte, Brazil (2011)



Death rates peaked during the second year of exposure.

Fig. 16. Distribution of the number of deaths by neoplasia versus duration of exposure since the date that the first antenna in each analyzed CT came into operation.

Dode AC, Leao MM, Tejo Fde A et al. Mortality by neoplasia and cellular telephone base stations in the Belo Horizonte municipality, Minas Gerais state, Brazil. *Sci Total Environ* (2011); 409(19):3649-3665.

Effects of Microwave RF Exposure on Fertility



Impaired Fertility in Fruit Flies



Insects are remarkably resistant to ionizing radiation and radioactivity.

They appear to be much more sensitive to the effects of microwave radio frequency exposures.

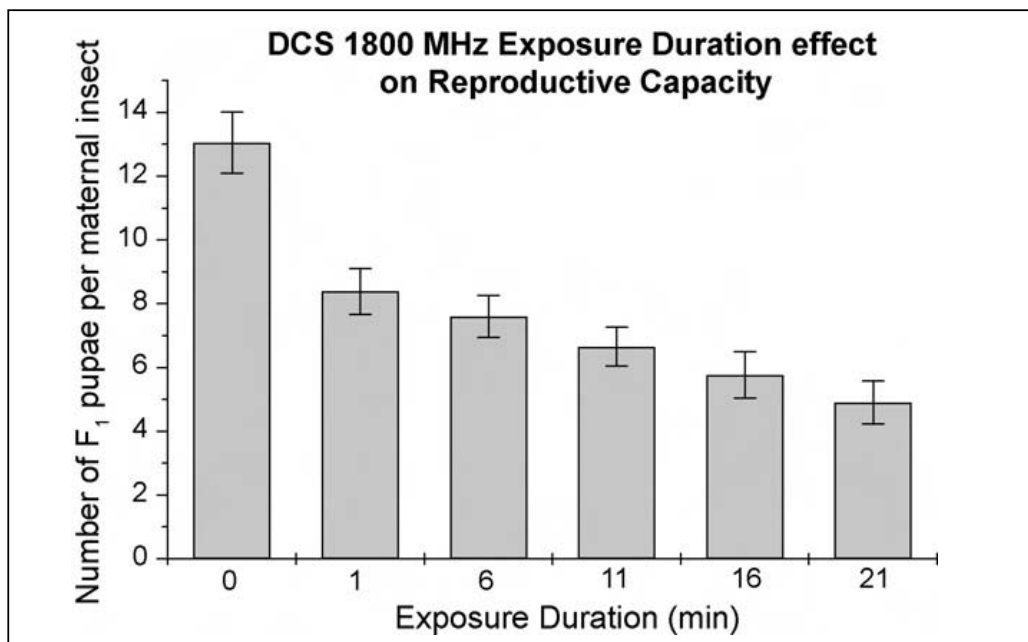
In a recent study, **fruit flies were exposed to 10 $\mu\text{W}/\text{cm}^2$ of GSM 900 MHz or 1800 MHz digital RF.**

This exposure level is 100 times lower than the FCC Guidelines of 1000 $\mu\text{W}/\text{cm}^2$

Exposures were for one single exposure intervals per day for five days, ranging from 1 to 21 minutes per day.

Panagopoulos DJ, Margaritis LH. The effect of exposure duration on the biological activity of mobile telephony radiation. *Mutat Res* (2010); 699(1-2):17-22.

Impaired Fertility in Fruit Flies



0 = control group, with no exposure.

Even at one minute of exposure per day, a significant decrease in fertility is seen.

Fig. 2. Reproductive capacity (mean number of F₁ pupae per maternal fly) of groups exposed to DCS 1800MHz radiation for different daily exposure durations (1, 6, 11, 16, and 21min) for five consecutive days, and of sham-exposed groups (no exposure).

Panagopoulos DJ, Margaritis LH. The effect of exposure duration on the biological activity of mobile telephony radiation. *Mutat Res* (2010); 699(1-2):17-22.

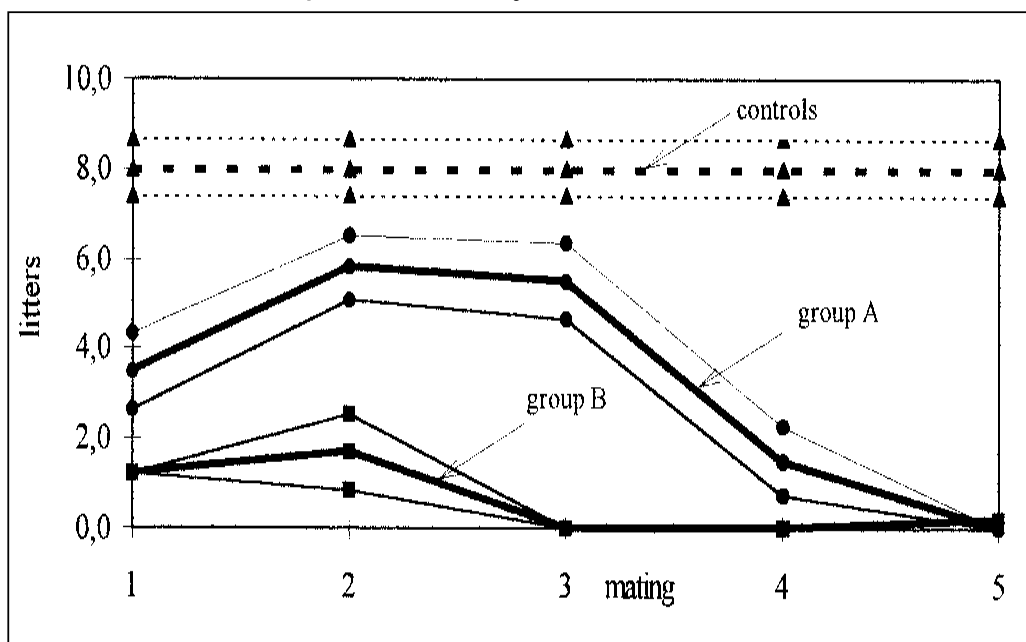
Impaired Fertility in Mammals



This is a Wistar rat.

A great deal of research has been done on the effects of microwave RF on laboratory animals.

Impaired Fertility in Female Mice



In one study, mice were kept in cages in a VHF/UHF antenna park in Thessaloniki, Greece.

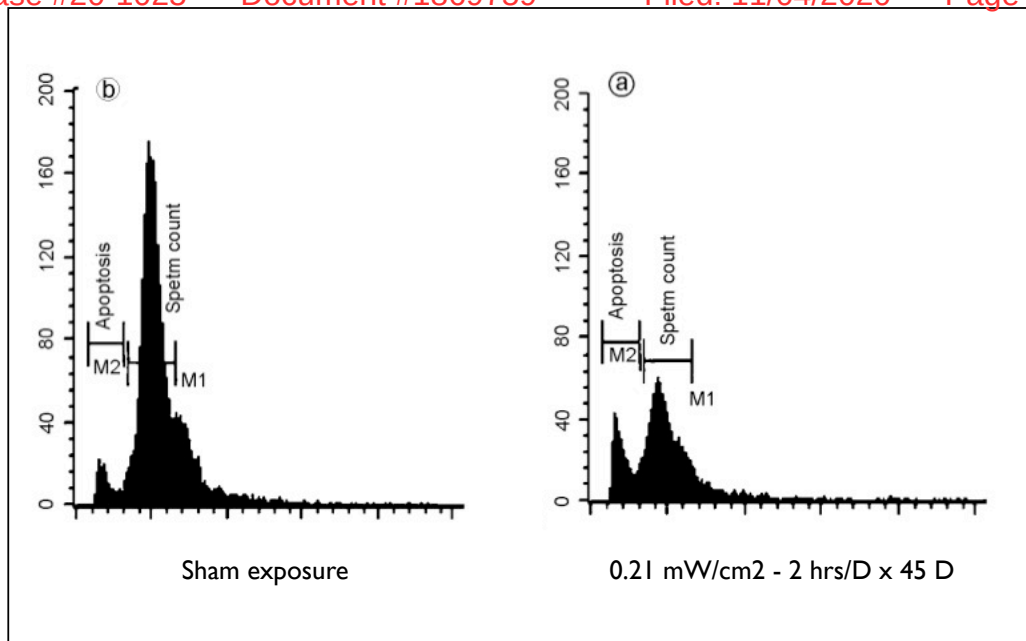
Power densities ranged between 0.168 to $1.053 \mu\text{W}/\text{cm}^2$ [reported as 168 – 1053 nanowatts/ cm^2]

This is about 1000 times lower than the FCC Guidelines of $600\text{--}1000 \mu\text{W}/\text{cm}^2$

With repeated matings, litter size decreased, until by the 5th mating, all the dams were infertile.

This infertility was irreversible.

Impaired Fertility in Male Rats



Reduced sperm production in male Wistar rats exposed to 10 GHz microwave RF.

0.21 mW/cm² = **one fifth** of the FCC Guidelines of 1 mW/cm²

OTHER EFFECTS: Increases in reactive oxygen species, increased free radical formation, decreased activity of glutathione peroxidase and superoxide dismutase, DNA strand breakage, increased apoptosis (cell death) in sperm cells, distortion of sperm structure, reduced testosterone levels, shrinkage of seminiferous tubules and testicular size, decreased number and weight of progeny.

Kesari KK, Kumar S, Behari J. Effects of radiofrequency electromagnetic wave exposure from cellular phones on the reproductive pattern in male Wistar rats.

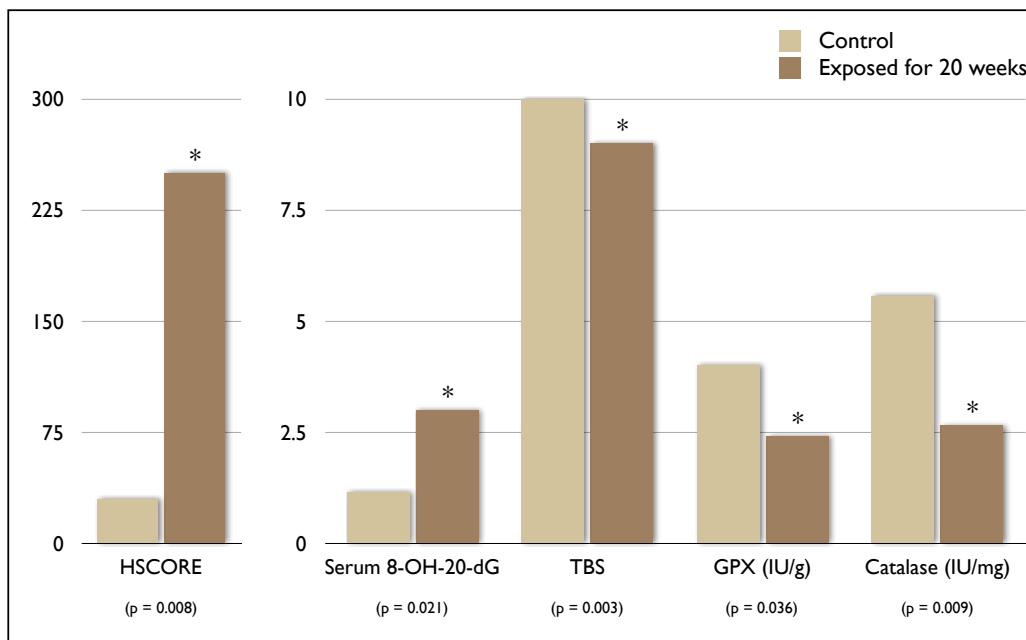
Appl Biochem Biotechnol (2011); 164(4):546-559.

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

Kumar S, Kesari KK, Behari J. Influence of microwave exposure on fertility of male rats. *Fertil Steril* (2011); 95(4):1500-1502.

Kumar S, Behari J, Sisodia R. Influence of electromagnetic fields on reproductive system of male rats. *Int J Radiat Biol* (2012); epub Nov 13:1-8

WiFi Exposure Damages Sperm With Oxidant Stress.



The rats were exposed to a Standard WiFi gateway, 24 hours a day for 20 days.

HSCORE = histological staining in testes for 8-OH-20-dG
[8-hydroxy-20-deoxyguanosine, **byproduct of DNA damage**]

Serum 8-OH-20-dG (ng/ml) [byproduct of DNA damage]

TBS = testicular biopsy score

9 = Much spermatogenesis, but germinal epithelium disorganized with marked sloughing or obliteration of lumen

GPX = glutathione peroxidase, an antioxidant (consumed by oxidative stress in exposed rats).

Atasoy HI, Gunal MY, Atasoy P, Elgun S, Bugdayci G. Immunohistopathologic demonstration of deleterious effects on growing rat testes of radiofrequency waves emitted from conventional Wi-Fi devices. *J Pediatr Urol* (2012); March 30.

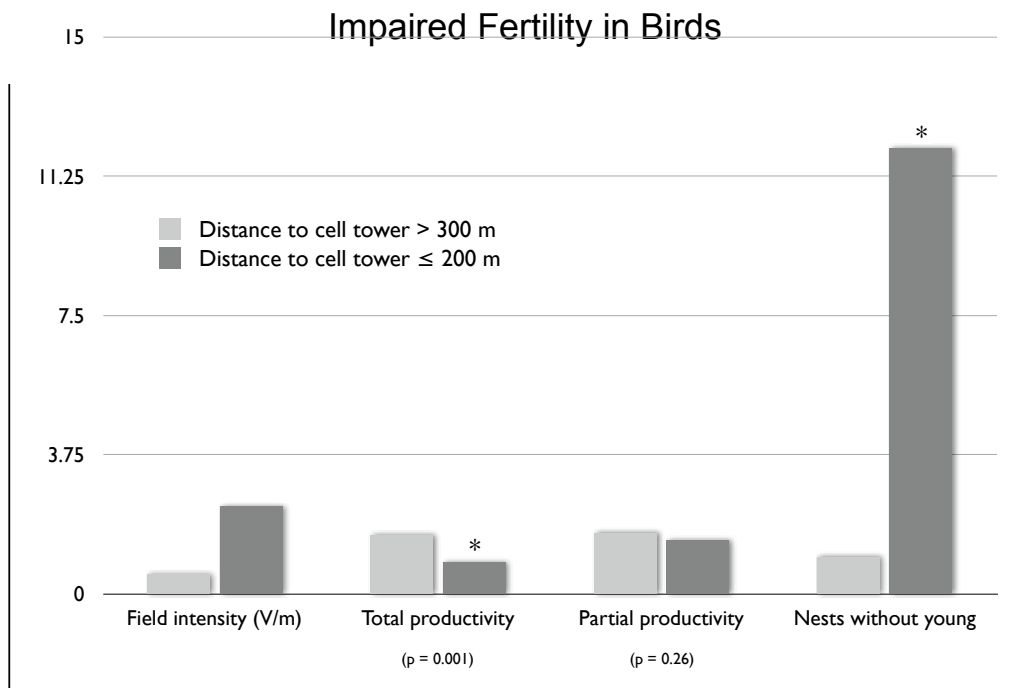
Impaired Fertility in Birds



In Valladolid, Spain, a study compared the productivity of storks nesting closer and farther from a cell phone tower site.

30 nests within 200 meters of the antennae, were compared with 30 nests greater than 300 meters from the antennae

Balmori A. Possible Effects of Electromagnetic Fields from Phone Masts on a Population of White Stork. *Electromagn Biol Med* (2005); 24(2):109-119.



Productivity was significantly reduced in birds in the high exposure group.

Average electric field intensity on nests within 200m = $2.36 \pm 0.82 \text{ V/m}$ (~ $1.48 \mu\text{W/cm}^2$)

This is more than 400 times less than the FCC Guidelines of 600–1000 $\mu\text{W/cm}^2$

Average electric field intensity on nests further than 300m = $0.53 \pm 0.82 \text{ V/m}$ (~ $0.07 \mu\text{W/cm}^2$).

Balmori A. Possible Effects of Electromagnetic Fields from Phone Masts on a Population of White Stork. *Electromagn Biol Med* (2005); 24(2):109-119.

Impaired Fertility in Amphibians



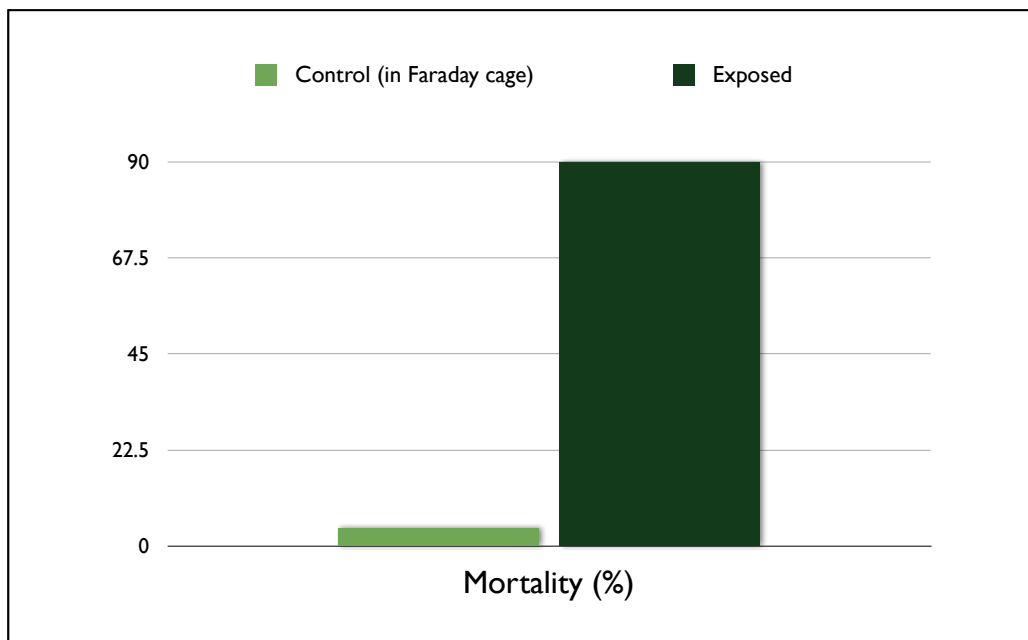
Eggs and tadpoles of the European common frog (*Rana temporaria*) were exposed to RF/EFM from several cell towers located at a distance of 140 meters.

Duration of exposure was 2 months (from egg phase to advanced tadpole stage).

Control groups were placed in same conditions, but contained in a faraday cage that shielded the eggs from RF exposure.

Balmori A. Mobile phone mast effects on common frog (*Rana temporaria*) tadpoles: the city turned into a laboratory. *Electromagn Biol Med* (2010a); 29(1-2):31-35.

Impaired Fertility in Amphibians

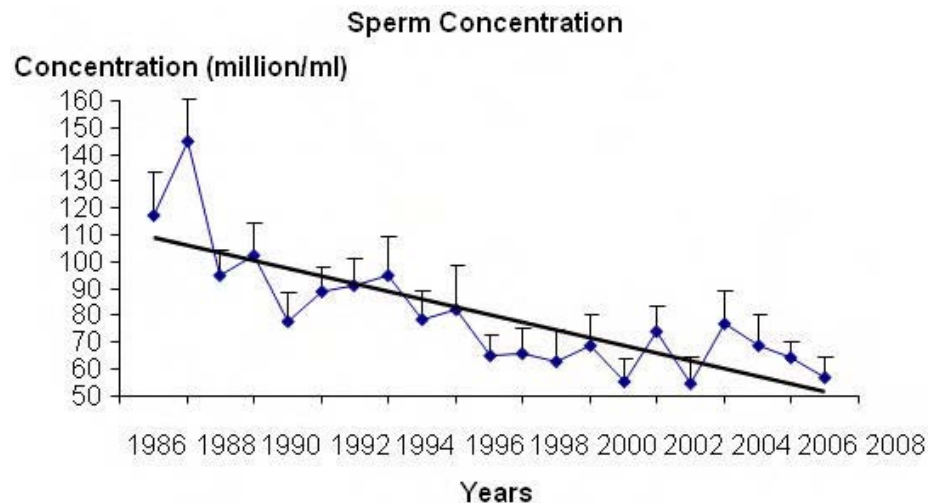


Exposure intensity 1.8 to 3.5 V/m (~ 0.8–3.2 $\mu\text{W}/\text{cm}^2$).

This is 200 times less than the FCC Guidelines of 600–1000 $\mu\text{W}/\text{cm}^2$

[In the exposed group (n = 70), low coordination of movements and asynchronous growth was observed in living specimens, resulting in both big and small tadpoles. In the control group (n = 70), growth was normal.]

Balmori A. Mobile phone mast effects on common frog (*Rana temporaria*) tadpoles: the city turned into a laboratory. *Electromagn Biol Med* (2010a); 29(1-2):31-35.

Figure 2. Sperm concentration in 975 sperm donors recruited over 20 years

Sperm counts have been dropping worldwide for the last several decades.

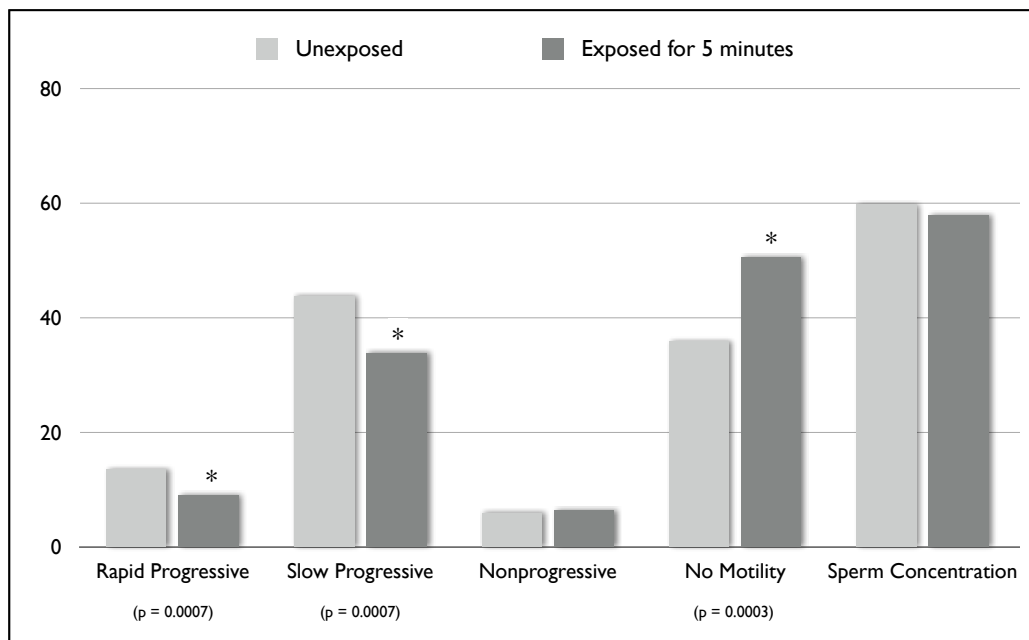
(e.g. In New Zealand, 2.5% per year for the last 20 years).

Pesticides have been implicated.

Some evidence suggests that microwave RF exposure may also play a role.

Shine R, Peek J, Birdsall M. Declining sperm quality in New Zealand over 20 years. *N Z Med J* (2008); 121(1287):50-56.

Cell Phone Transmissions Decrease Sperm Motility in Vitro



Samples of human sperm received 5 minutes exposure, 10 cm from a transmitting GSM 900 MHz cell phone.

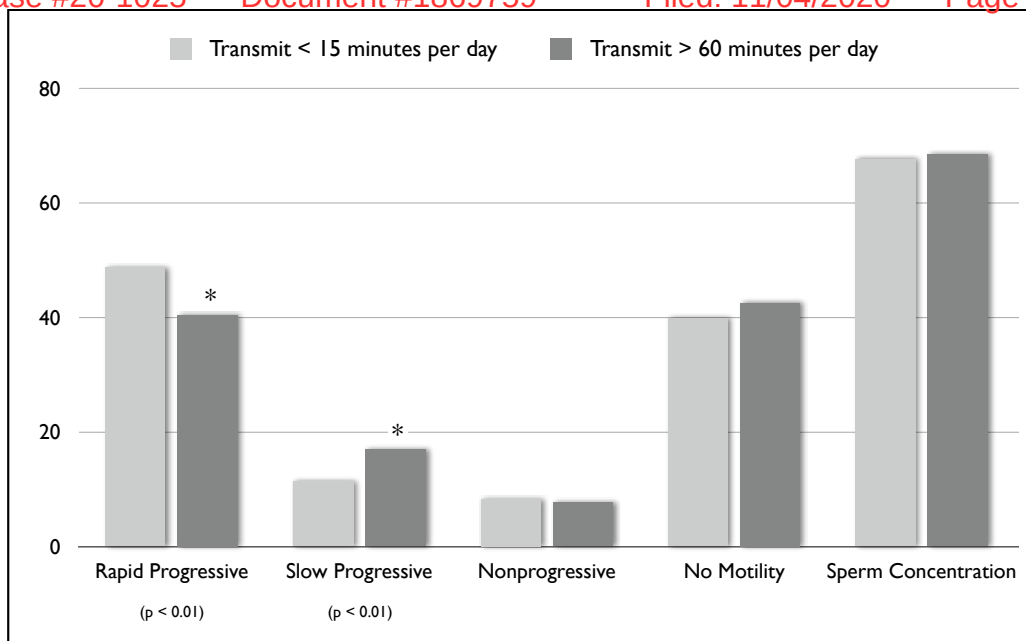
Average power density of exposure: 20 $\mu\text{W}/\text{cm}^2$

This is 30 times less than the FCC Exposure Guideline of 600 $\mu\text{W}/\text{cm}^2$

(Y axis = values in %)

Eroglu O, Oztas E, Yildirim I et al. Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study. *Arch Med Res* (2006); 37(7):840-843.

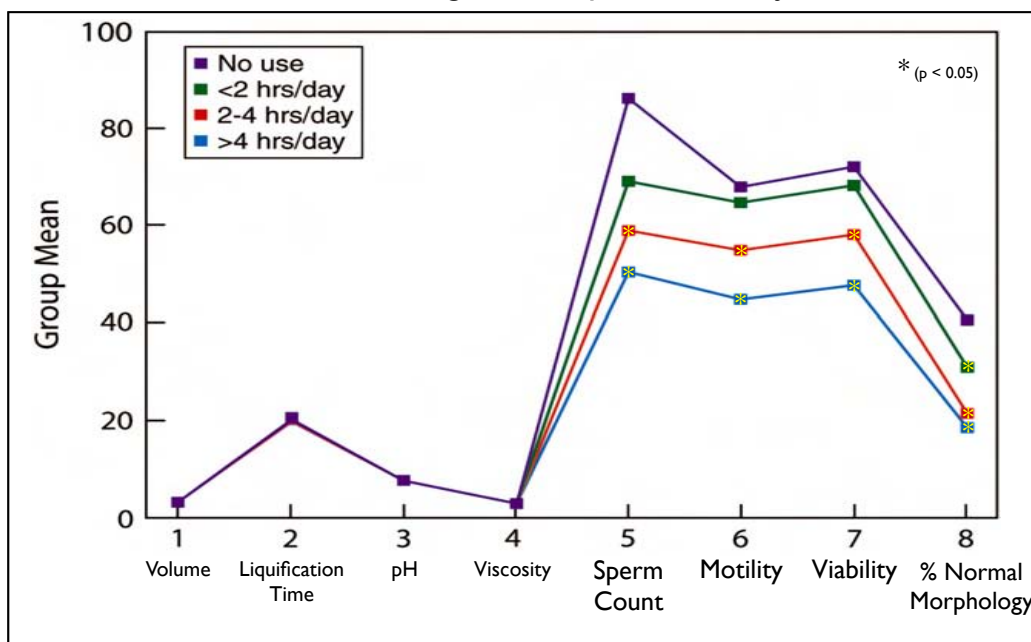
Cell Phone Use Decreases Sperm Motility in Vivo



Semen analysis performed on 371 men at a university clinic.
Health questionnaire included query of cell phone use habits.
(Y axis = values in %)

Fejes I, Zavaczki Z, Szollosi J et al. Is there a relationship between cell phone use and semen quality? *Arch Androl* (2005); 51(5):385-393.

Cell Phone Use Degrades Sperm Quality in Vivo



Three hundred sixty-one men undergoing infertility evaluation were divided into four groups according to their active cell phone use:

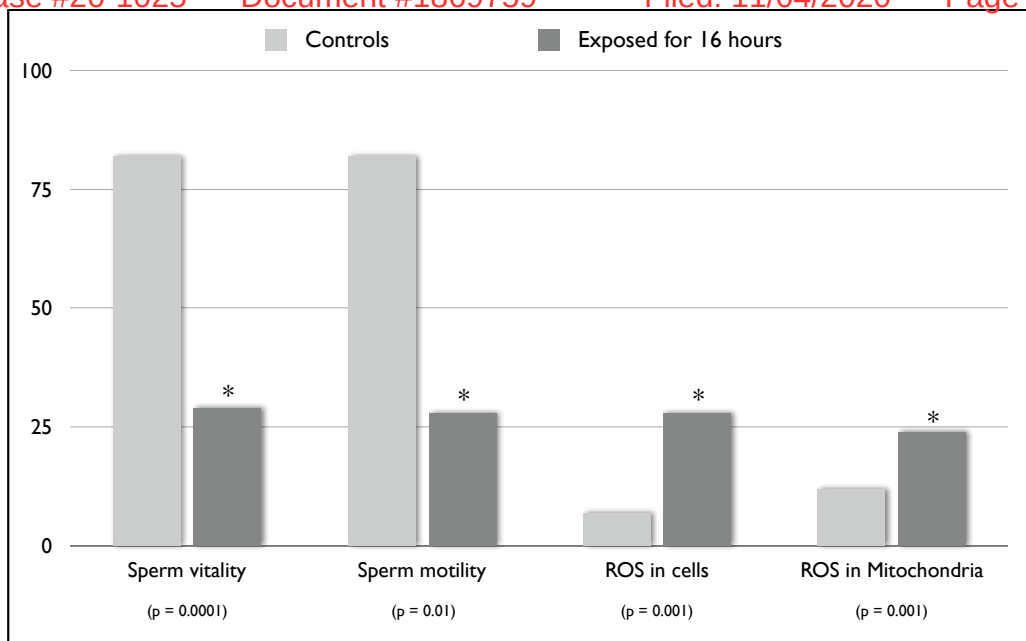
group A: no use; group B: <2 h/day; group C: 2-4 h/day; and group D: >4 h/day.

With greater than two hours a day of reported talk time, significant reduction in **sperm count, motility, viability, and % normal morphology** were observed.

[One can assume that with texting rather than talking, the data might be even worse . . . as the phone antenna will be closer to the testes.]

Agarwal A, Deepinder F, Sharma RK, Ranga G, Li J. Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study. *Fertil Steril* (2008); 89(1):124-128.

Isothermal Exposure to 1.8 GHz RF Damages Sperm



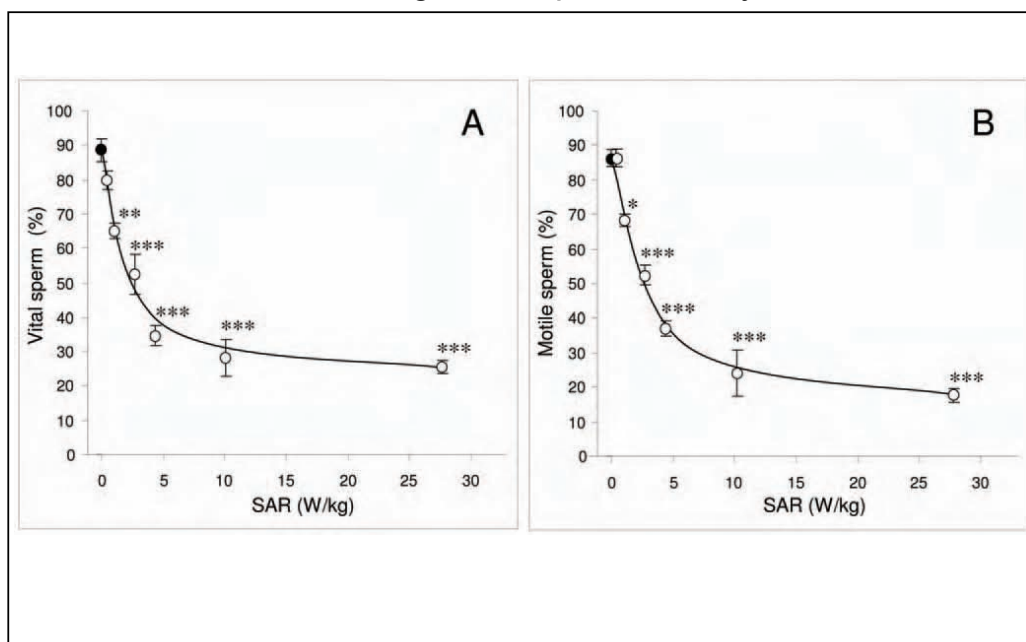
Sperm exposed for 16 hours in vitro to 1.8 GHz (SAR = 27.5 W/kg) @ 21°C (isothermal conditions).

Sperm damage correlates with increased free radical (ROS) production.

Values in %.

De Iuliis GN, Newey RJ, King BV, Aitken RJ. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. *PLoS One* (2009); 4(7):e6446 (1-9).

1.8 GHz RF Degrades Sperm Quality In Vitro



1.8 GHz RF at various intensities for 16 hours @ 21°C

This is an isothermal exposure

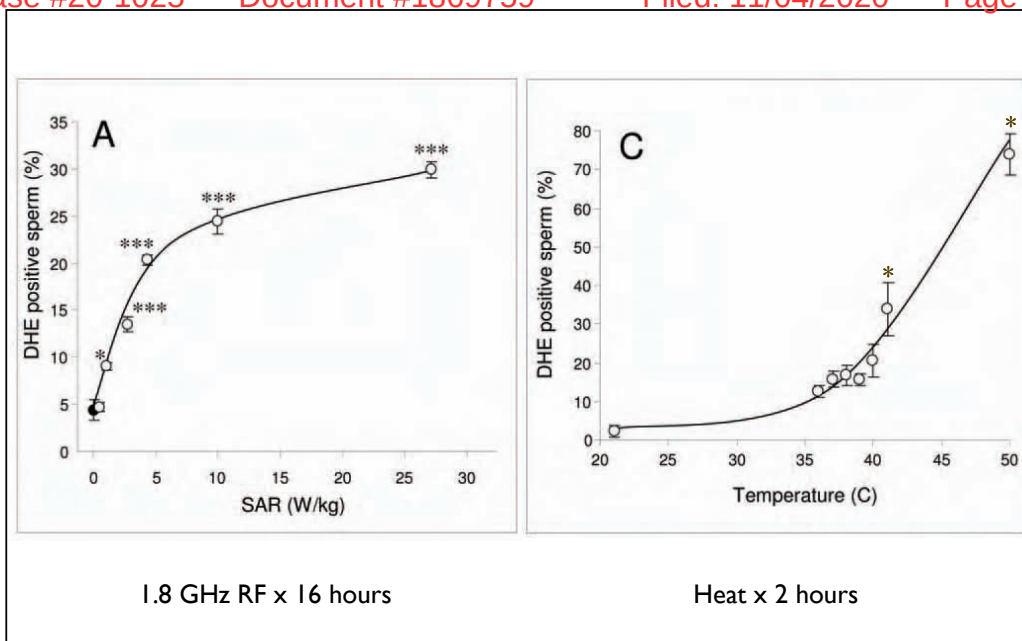
Sperm vitality and motility are significantly detracted at SAR = 1 W/kg and above

Figure 2. RF-EMR exposure reduces motility and vitality of human spermatozoa, in an SAR dependent manner. Percoll-purified spermatozoa (5×10^6 cells) were suspended in 1 ml BWB in a 35 mm Petri dish and placed within the waveguide while control cells (closed circles) were placed outside the waveguide. Cells in the waveguide were exposed to 1.8 GHz RF-EMR at SAR levels of 0.4, 1.0 2.8 4.3 10.1 and 27.5 W/kg (open circles) for 16 h at 21°C. Both vitality and motility were reduced in a dose dependent manner.

A, Vitality was significantly reduced at a SAR of 1.0 W/kg from $89\% \pm 3\%$ to $65\% \pm 1\%$ (**p.0.01).

B, Motility was also significantly reduced at a SAR of 1.0 W/kg from $86\% \pm 2\%$ to $68\% \pm 2\%$ (*p.0.05). All results are based on 4 independent samples.

ROS Production – RF versus Thermal



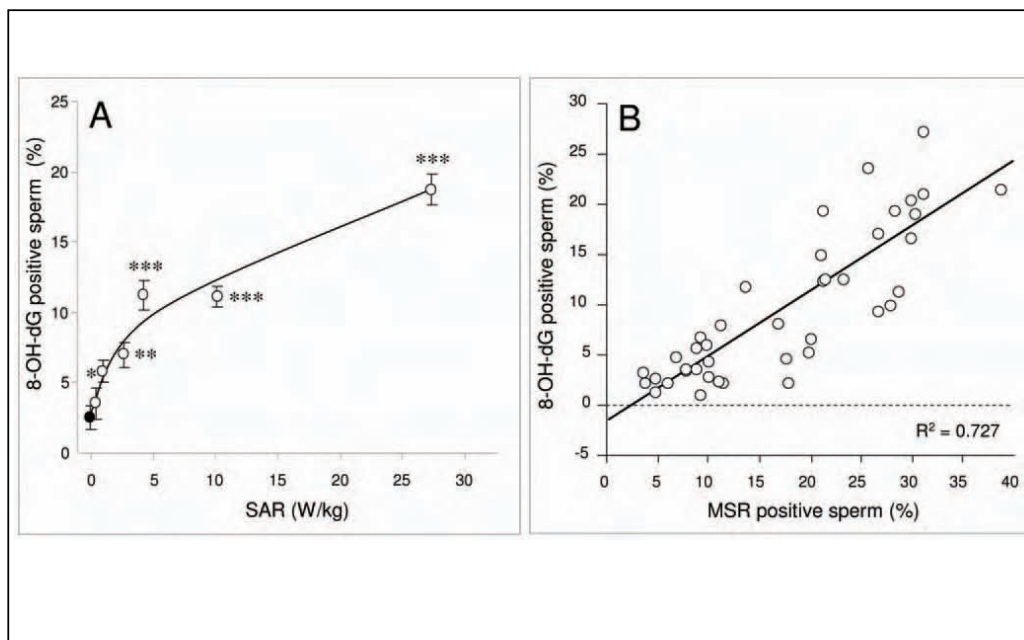
A. ROS generation (DHE response) was significantly increased from control levels after exposure to 1.0 W/kg (*p, 0.05) and above (***p, 0.001).

C. In order to control for thermal effects, the impact of temperature of cellular ROS generation was monitored; a significant increase in ROS generation was observed as temperatures rose above 40°C (p, 0.001).

Figure 3. RF-EMR induces ROS generation in human spermatozoa, in an SAR-dependent manner unrelated to thermal effects.

De Iuliis GN, Newey RJ, King BV, Aitken RJ. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. *PLoS One* (2009); 4(7):e6446 (1-9).

Oxidative Damage To Sperm DNA From 1.8 GHz RF Exposure



1.8 GHz RF x 16 hours @ 21°C isothermal.

A) As the power levels were increased, the amount of oxidative DNA damage expressed also increased.

A significant amount of oxidative DNA damage was observed in cells exposed to 2.8 W/kg (*p, 0.05) RF-EMR and above (**p, 0.01; ***p, 0.001).

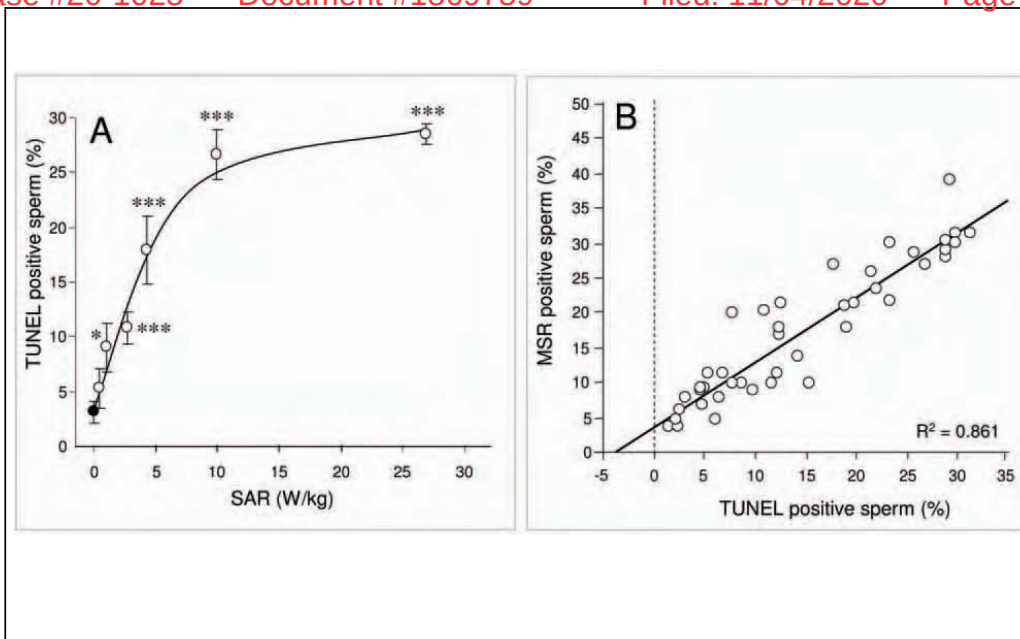
B) The levels of 8-OH-dG expression were positively correlated with the levels of ROS generation by the mitochondria ($R^2 = 0.727$).

Figure 4. RF-EMR induces oxidative DNA damage in human spermatozoa.

De Iuliis GN, Newey RJ, King BV, Aitken RJ. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. *PLoS One* (2009); 4(7):e6446 (1-9).

RF Damages Sperm by Increasing Oxidative Stress

USCA Case #20-1025 Document #1869759 Filed: 11/04/2020 Page 311 of 427



A) Significant levels of DNA fragmentation was observed in exposed spermatozoa at 2.8 W/kg (*p,0.05) and above (**p,0.001).

B) DNA fragmentation was positively correlated with ROS production by the mitochondria as monitored by MSR. ($R^2 = 0.861$).

Figure 5. RF-EMR induces DNA fragmentation in human spermatozoa.

De Iuliis GN, Newey RJ, King BV, Aitken RJ. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. *PLoS One* (2009); 4(7):e6446 (1-9).

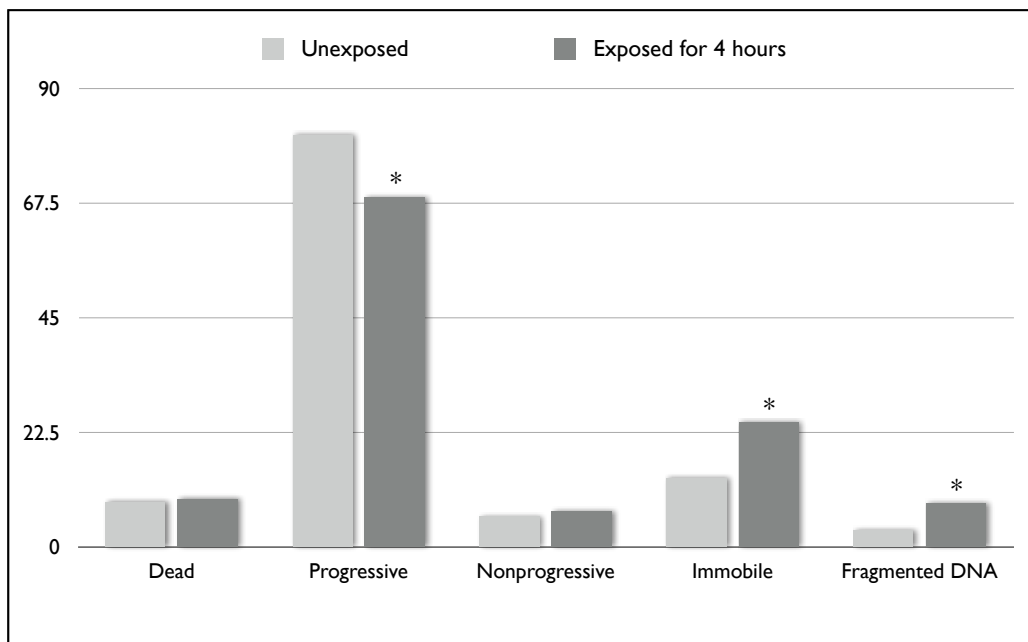


Motile spermatozoa in semen were incubated at room temperature,
3 cm below laptop computer (e.g. lap distance)
4 hours of exposure.

Control incubated in similar conditions, without presence of the computer.

Avendano C, Mata A, Sanchez Sarmiento CA, Doncel GF. Use of laptop computers connected to internet through Wi-Fi decreases human sperm motility and increases sperm DNA fragmentation. *Fertil Steril* (2012); 97(1):39-45.

Sperm Damage From Laptop WiFi



Power density ranged 0.45 to 1.05 $\mu\text{W}/\text{cm}^2$

[This is roughly **1000 times less** than the FCC exposure limit of 1000 $\mu\text{W}/\text{cm}^2$]

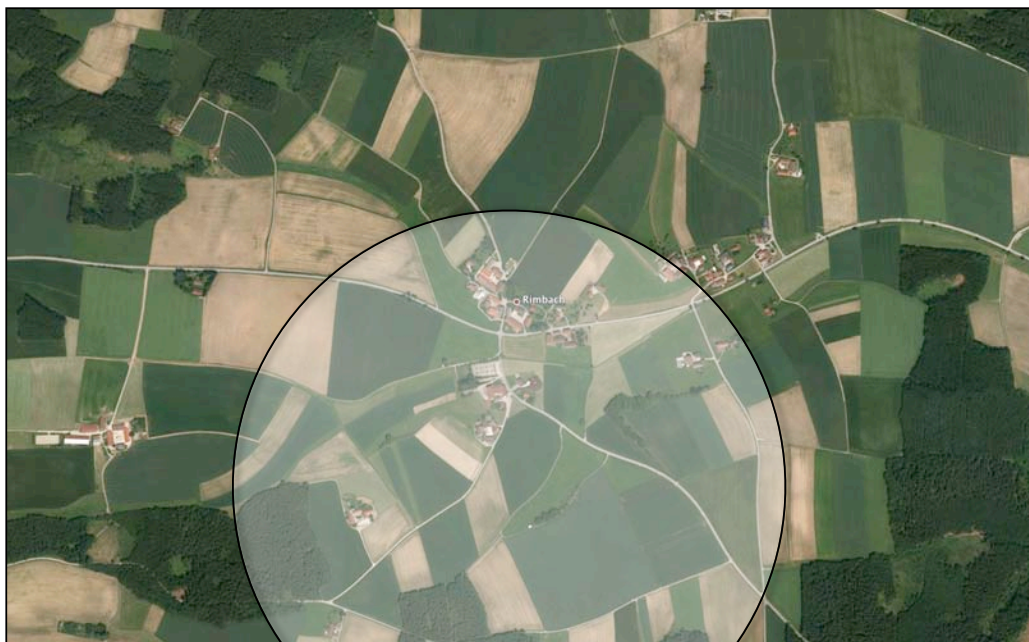
Avendano C, Mata A, Sanchez Sarmiento CA, Doncel GF. Use of laptop computers connected to internet through Wi-Fi decreases human sperm motility and increases sperm DNA fragmentation. *Fertil Steril* (2012); 97(1):39-45.

Hormonal; RF and Hormones, Alterations in Hormone
Physiology; Dr. Paul Dart MD. (Petitioner); 2013

Alterations in Hormone Physiology



Rimbach, Bavaria (2004 - 2005)



In spring of 2004 a GSM cell tower was installed near Rimbach, Bavaria (population ~ 2000).

Prior to activation of the antenna, the town residents were asked to participate in a mass screening.

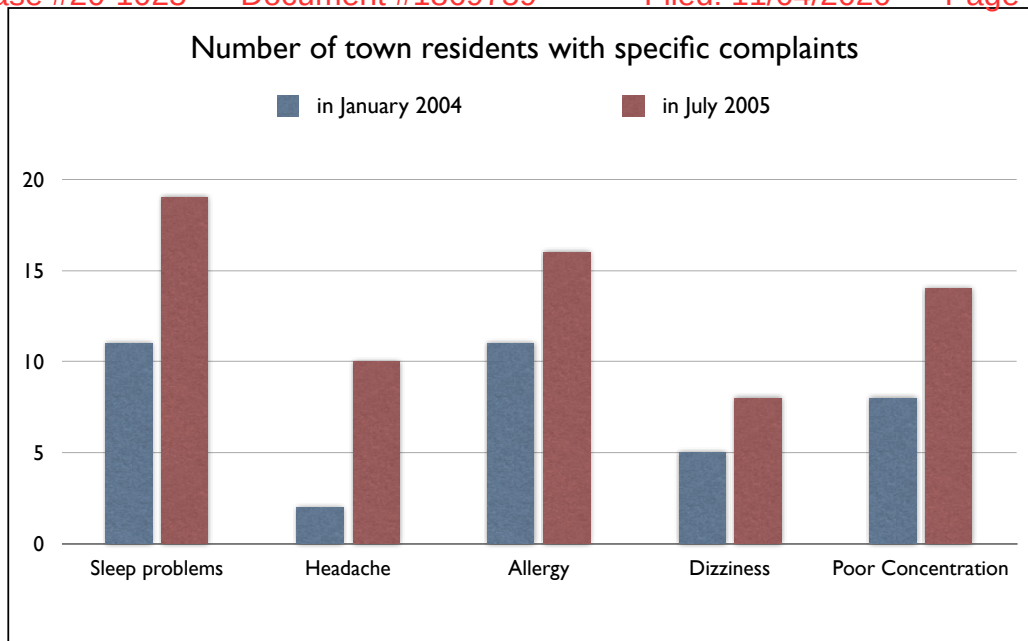
Urine levels of the stress hormones adrenaline, noradrenaline, dopamine, and phenylethylamine were measured in January/February 2004, and again in July 2004, January 2005, and July 2005.

A medical history and symptom questionnaire was also administered.

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Buchner K EH. Changes of Clinically Important Neurotransmitters under the Influence of Modulated RF Fields--A Long-term Study under Real-life Conditions. *Umwelt-Medizin-Gesellschaft* (2011); 24(1):44-57.

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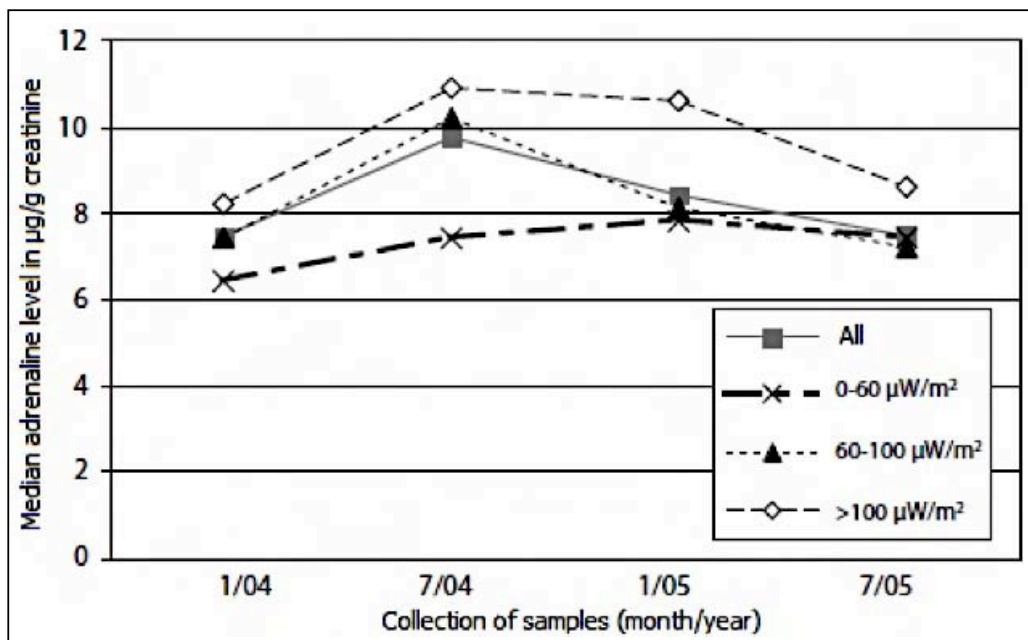


Here we see some symptom scores before tower activation (blue) and after a year of tower transmission (red)
Some health complaints increased over the course of the study.

Buchner K EH. Changes of Clinically Important Neurotransmitters under the Influence of Modulated RF Fields--A Long-term Study under Real-life Conditions. *Umwelt-Medizin-Gesellschaft* (2011); 24(1):44-57.

Abstract: This follow-up of 60 participants over one and a half years shows a significant effect on the adrenergic system after the installation of a new cell phone base station in the village of Rimbach (Bavaria). After the activation of the GSM base station, the levels of the stress hormones adrenaline and noradrenaline increased significantly during the first six months; the levels of the precursor dopamine decreased substantially. The initial levels were not restored even after one and a half years. As an indicator of the dysregulated chronic imbalance of the stress system, the phenylethylamine (PEA) levels dropped significantly until the end of the study period. The effects showed a dose-response relationship and occurred well below current limits for technical RF radiation exposures. Chronic dysregulation of the catecholamine system has great relevance for health and is well known to damage human health in the long run.

Adrenaline levels



Results were stratified by in-home exposure levels (mW/m^2) in three cohorts.

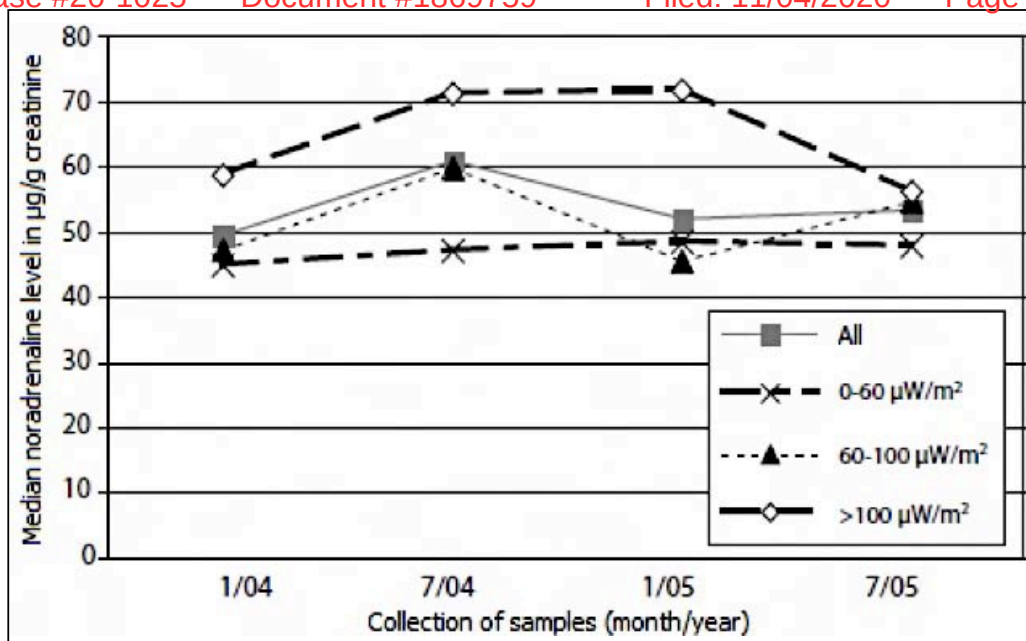
Hormone levels graphed for each exposure cohort.

Levels of the stress hormone adrenaline rose after the transmitter became active.

In the highest exposure cohort adrenaline levels never returned to pre-exposure baseline.

Fig. 3: Median adrenaline levels for all participating citizens of Rimbach whose cell phone base station exposure was above 100 $\mu\text{W}/\text{m}^2$, between 60 and 100 $\mu\text{W}/\text{m}^2$, or up to 60 $\mu\text{W}/\text{m}^2$. The power density levels refer to peak values of the GSM radiation exposure in front of a given residence.

Noradrenaline levels



Noradrenaline levels also rose after the transmitter became active.

They never returned to pre-exposure baseline.

Fig. 7: Median noradrenaline levels in all participating citizens of Rimbach as a function of GSM power density levels (peak values)

Effect of cordless DECT phones.

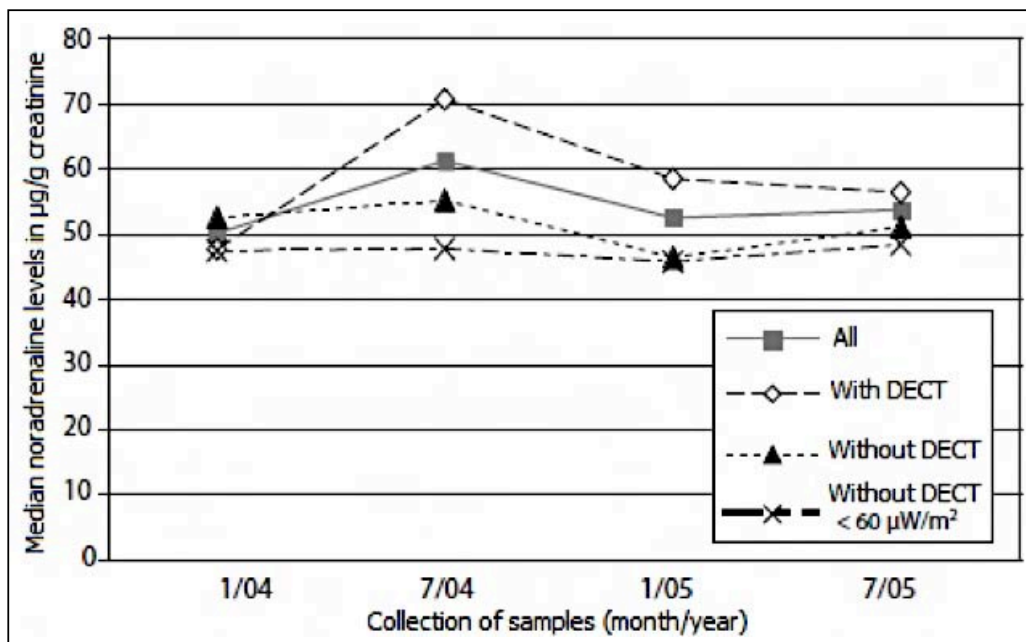
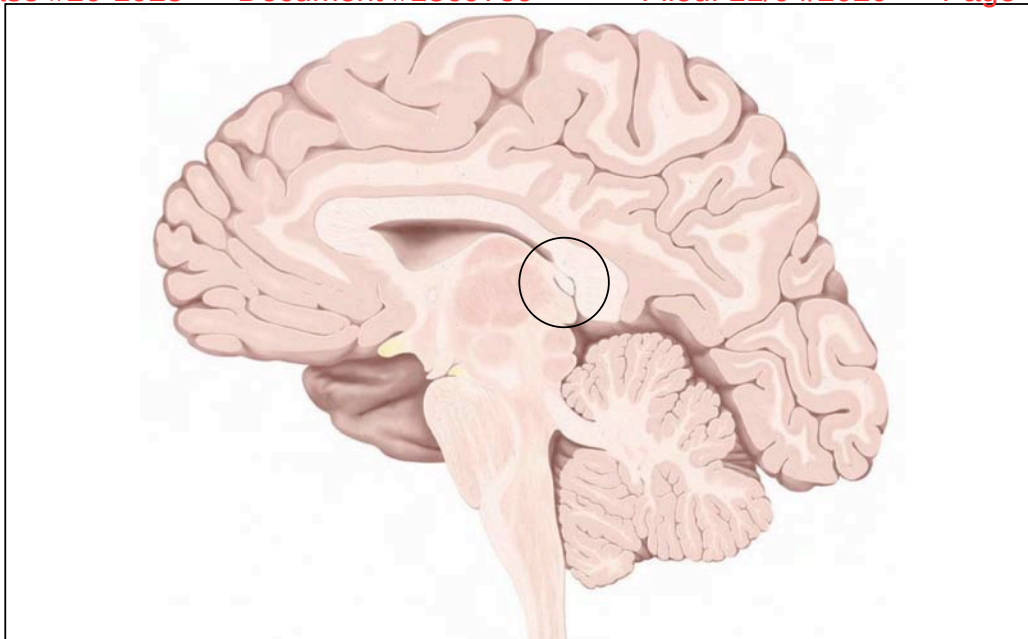


Fig. 8: Median noradrenaline values for subjects who had a DECT phone or other wireless devices at home, for those without indoor wireless devices, as well as for subjects without indoor wireless devices and with a GSM radiation exposure up to 60 $\mu\text{W}/\text{m}^2$ (peak value measured in front of residence)

Buchner K EH. Changes of Clinically Important Neurotransmitters under the Influence of Modulated RF Fields--A Long-term Study under Real-life Conditions. Umwelt-Medizin-Gesellschaft (2011); 24(1):44-57.

Abstract: This follow-up of 60 participants over one and a half years shows a significant effect on the adrenergic system after the installation of a new cell phone base station in the village of Rimbach (Bavaria). After the activation of the GSM base station, the levels of the stress hormones adrenaline and noradrenaline increased significantly during the first six months; the levels of the precursor dopamine decreased substantially. The initial levels were not restored even after one and a half years. As an indicator of the dysregulated chronic imbalance of the stress system, the phenylethylamine (PEA) levels dropped significantly until the end of the study period. The effects showed a dose-response relationship and occurred well below current limits for technical RF radiation exposures. Chronic dysregulation of the catecholamine system has great relevance for health and is well known to damage human health in the long run.

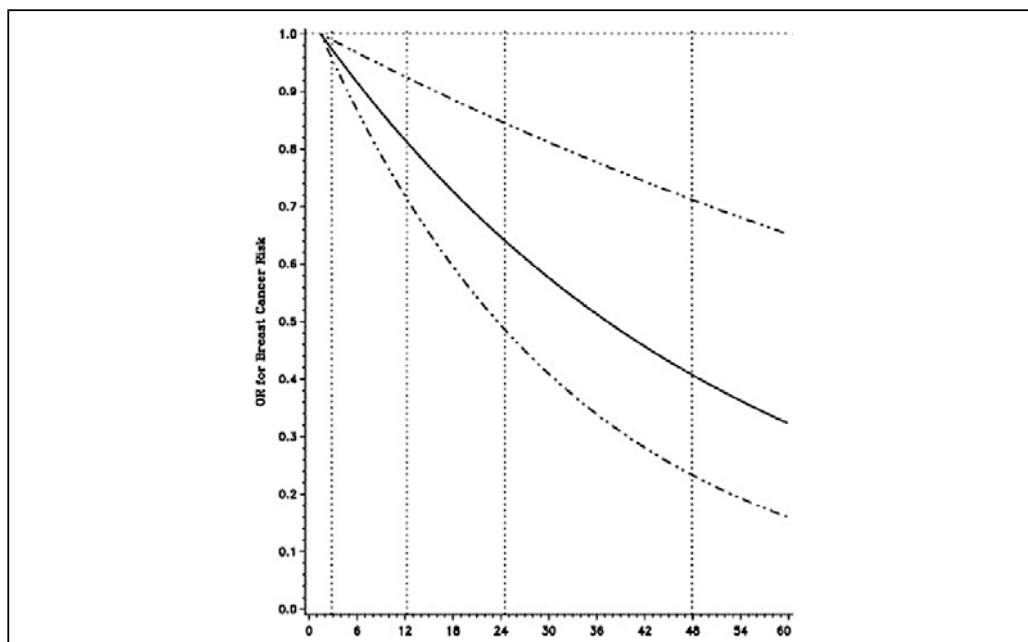


The pineal gland secretes melatonin. Ambient light suppresses melatonin secretion. So melatonin secretion is high during the night-time hours, peaking shortly after midnight. **Higher melatonin levels are part of what makes us feel “sleepy” at night.**

Exposure to light during the night-time hours will lead to a rapid suppression of melatonin secretion by the pineal gland, and this can cause disruption of sleep and derangement of the circadian rhythm.

Melatonin is one of the most potent anti-oxidant molecules in the human body, and acts to reduce reactive oxidative processes in the body. Melatonin can quench the damaging free radical activity produced by inflammation. The presence of elevated melatonin at night is therefore a key factor in the healing and rejuvenating functions that we associate with “a good night’s sleep”.

Melatonin lowers risk of breast cancer.



[Figure 1. Smoothing spline plot for aMT6s level (ng/mg creatinine) in relation to breast cancer risk among postmenopausal women. 95% CIs are indicated by dotted lines.]

Melatonin is also protective against the growth of cancer cells, and disruption of the circadian melatonin cycle has been shown to lead to increased tumor growth in a variety of cancer types.

Women who have lower levels of nocturnal melatonin are at greater risk for developing breast cancer.

In 2007 the International Agency for Research on Cancer declared night shift work to be a probable carcinogen due to increased breast cancer risk..

Schwarzenburg Short Wave Radio Broadcast Tower – 1998

USCA Case #20-1025 Document #1869759 Filed: 11/04/2020 Page 318 of 427



RF exposure can also lower melatonin levels.

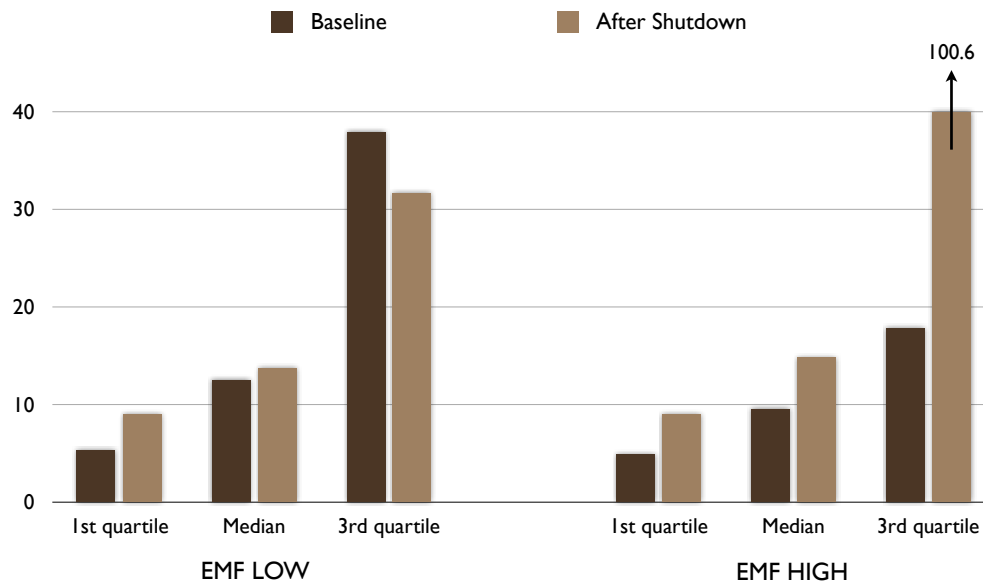
Schwarzenburg experiment: Decommissioning the Swiss national short-wave radio transmitter of Schwarzenburg, about 20 km south of the Swiss Capital city of Berne, transmitting since 1939. It operated at frequencies of 3 to 30 MHz, with a maximum power of two times 150 kW.

Figure 1. Map of the Schwarzenburg area showing the location of the transmitter, the H-field measurement points and the location of the zones A, B, C and R. The diameters of the circles around the measurement points indicate the 24 hour average magnetic field strengths, as measured between August 1992 and August 1993. (Reproduced with approval from swisstopo (BA046633.))

Abelin T, Altpeter E, Roosli M. Sleep Disturbances in the Vicinity of the Short-Wave Broadcast Transmitter Schwarzenburg. *Somnologie* (2005); 9:203-209.

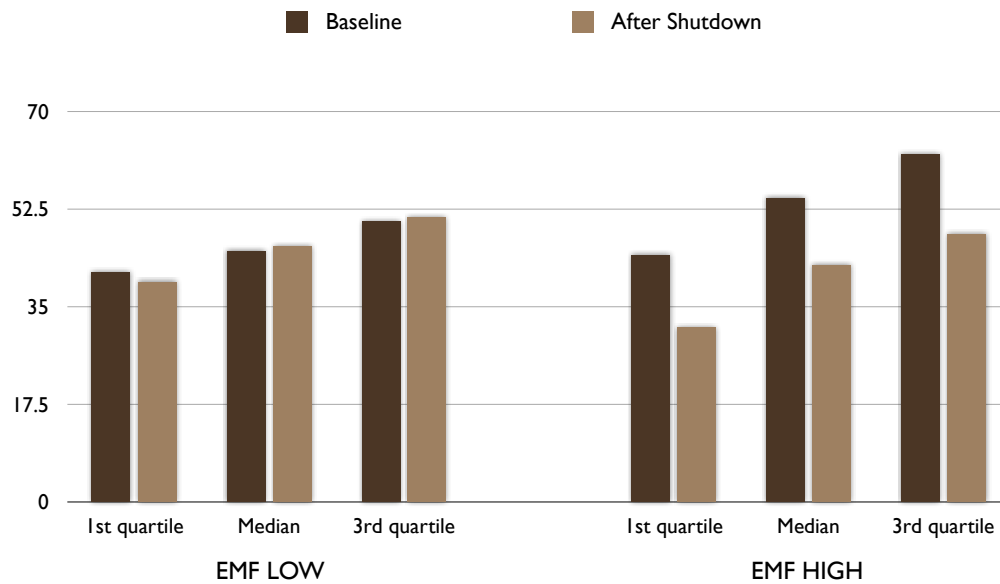
Altpeter ES, Roosli M, Battaglia M, Pfluger D, Minder CE, Abelin T. Effect of short-wave (6-22 MHz) magnetic fields on sleep quality and melatonin cycle in humans: the Schwarzenburg shut-down study. *Bioelectromagnetics* (2006); 27(2):142-150.

Melatonin Excretion (pg/ml)



Altpeter ES, Roosli M, Battaglia M, Pfluger D, Minder CE, Abelin T. Effect of short-wave (6-22 MHz) magnetic fields on sleep quality and melatonin cycle in humans: the Schwarzenburg shut-down study. *Bioelectromagnetics* (2006); 27(2):142-150.

Morning Fatigue (0 - 100 Scale)



Altpeter ES, Roosli M, Battaglia M, Pfluger D, Minder CE, Abelin T. Effect of short-wave (6-22 MHz) magnetic fields on sleep quality and melatonin cycle in humans: the Schwarzenburg shut-down study. *Bioelectromagnetics* (2006); 27(2):142-150.

Prenatal & Children; Fetal Radiofrequency Radiation Exposure From 800-1900 Mhz-Rated Cellular Telephones Affects Neurodevelopment and Behavior in Mice. Scientific Reports. (Aldad, Taylor et al); 2012



SUBJECT AREAS:
DEVELOPMENT
PATTERN FORMATION
BIOPHYSICS
ANIMAL BEHAVIOUR

Received
13 July 2011

Accepted
17 February 2012

Published
15 March 2012

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Fetal Radiofrequency Radiation Exposure From 800-1900 Mhz-Rated Cellular Telephones Affects Neurodevelopment and Behavior in Mice

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

To date, 3–7% of school-aged children suffer from attention deficit hyperactivity disorder (ADHD)¹. Children diagnosed with ADHD are at greater risk for low academic achievement, poor school performance, and delinquent behavior inconsistent with their developmental level^{2,3}. The diagnosis of ADHD has increased at an average rate of 3% per year since 1997, making the condition a growing public health concern¹. The behavioral problems in ADHD have been associated with neuropathology localized primarily to the prefrontal cortex. Children with ADHD have a reduction in prefrontal cortex volume, a reduction in gray and white matter, and asymmetry^{4,5}. These children also have a deficit in working memory associated with inattention and controlled by activity of neurons in the prefrontal cortex⁶. A recent study showed that poor attention and low working memory capacity may be due to the inability to override the involuntary capture of attention by irrelevant information⁷. This too is controlled by the prefrontal cortex, as the shifting of one's attention voluntarily is driven by “top-down” signals in the prefrontal cortex while the involuntary capture of attention depends on “bottom-up” signals from both subcortical structures and the visual cortex⁷.

The etiology of ADHD remains unknown and growing evidence suggests that it is not solely due to genetic factors⁸. Risk factors include family psychiatric history, socioeconomic status, gender, and smoking during pregnancy^{9,10}. A recent epidemiologic study found an association between prenatal cellular telephone exposure and subsequent behavioral problems in the exposed offspring¹¹. This association is important given the increasing number of cellular phone users worldwide, reaching approximately four billion as of December 2008¹². However, evidence of direct causation is lacking.

The specific absorption rate (SAR) is a measure of tissue radiation exposure. The European Union has set a SAR limit of 2.0 W/kg and in the United States this limit is set at 1.6 W/kg¹³. The *in-utero* effects of radiation exposure



within this SAR limit on neurodevelopment remain unknown. To determine if prenatal exposure to radiofrequency radiation leads to impaired memory or behavior after birth, we performed behavioral and electrophysiological studies in mice exposed *in-utero* to 800–1900 Mhz radiofrequency radiation from cellular telephones.

Results

In order to determine if *in-utero* cell phone radiation exposure affects behavior we chose to conduct a battery of tests that identify impairments in memory, hyperactivity, anxiety, and fear, which are often associated with ADHD. Thirty-three female mice were exposed throughout gestation (days 1–17) to radiation from muted and silenced 800–1900 Mhz cellular phones with a SAR of 1.6 W/kg. The phones were positioned above each cage over the feeding bottle area at a distance of 4.5–22.3 cm from each mouse, depending on the location of the animal within the cage, and placed on an uninterrupted active call for the duration of the trial. A control group of forty-two female mice was kept concurrently under the same conditions, however using a deactivated phone. Parturition was not different between groups and occurred at 19 days $\pm$ 1 day. In order to evaluate memory in the exposed and unexposed mice, 161 progeny were given a standard object recognition memory test in three different cohorts at 8, 12, and 16 weeks of age (82 experimental and 79 control mice). The mice were allowed to explore two identical objects for 15 minutes per day for two days and on the third day one object was replaced with a novel object. On day 3 the mice were filmed for 5 minutes exploring the novel and familiar objects. Three observers, blinded to the treatment, viewed the footage and recorded the exploration time for the novel and familiar objects. The preference index was defined as the time spent exploring the new object divided by the time spent exploring both the new and old object, multiplied by one hundred. A decrease in preference index indicates diminished memory. The preference index of the experimental group at 8, 12, and 16 weeks was less than the control and the results were significant at each time point [Figure 1]. The mean preference index in the exposed group was 56.8, 69.4 and 63.5 compared to 66.5, 71.7, and 71.2 in the control group at 8, 12 and 16 weeks, respectively. The experimental group had a cumulative mean preference index of 63.0% and the control group 69.9% ($p = 0.003$, $n=161$, t test). Compared to the control group, the exposed mice had a significantly lower mean preference index suggesting impairment in memory [Figure 1]. In order to ensure that our findings are in fact due to memory deficits and not distractibility or hyperactivity we calculated the percent time spent idle - not exploring either of the objects. The mean idle time in the exposed group was 90.06, 90.53, and 96.48 compared to 92.12, 91.89, and 97.07 in the control group at 8, 12 and 16 weeks, respectively. The control group had a cumulative mean idle time of 90.8% while the experimental group had a cumulative mean idle time of 90.4% and the difference between the two groups was not statistically significant ($p = .58$).

To explore fearful behavior we performed the light/dark box test measuring hyperactivity/anxiety and the step down assay assessing fear of exploring the environment. The light/dark box test measures anxiety using a rodent's natural aversion to bright light¹⁴. The box contained two compartments: one white compartment that was illuminated and one black compartment that remained dark. The number of transitions between the two compartments was used to determine locomotion and in turn hyperactivity¹⁵. Anxious behavior is measured by recording the time spent in each compartment¹⁵. A total of 141 progeny were given the light/dark box test in three different cohorts at 12, 15, and 18 weeks of age (71 experimental and 70 control mice). Each mouse was placed in the light/dark box for 5 minutes and filmed. Three observers, blinded to the treatment regimen, viewed the footage and recorded the time spent in the dark compartment along with the number of transitions between each compartment. The

average number of transitions in the experimental group at 12, 15, and 18 weeks was fewer than in respective controls and the results were significant at each time point [Figure 1]. The average number of transitions in exposed mice was 29.9, 32.5 and 14.8 compared to 23.9, 13.8, and 6.5 in the control group at 12, 15 and 18 weeks, respectively. The experimental group showed a cumulative mean of 24.4 transitions and the control group showed a mean of 16.4 transitions ($p < 0.001$). Compared to the control group, the greater number of transitions between the two compartments in the experimental group suggested hyperactive behavior [Figure 1].

To identify whether anxiety might be a factor contributing to the behavioral phenotype reported in the light/dark box experiment, we first compared the duration of time in the dark versus the time spent in the light. An increased time in the dark indicates anxious behavior¹⁵. At 12, 15, and 18 weeks the experimental group spent less time in the dark and the results were significant at each time point [Figure 1]. The duration of time in darkness of the exposed group was 210.8, 187.0 and 235.8 seconds compared to 225.6, 215.5 and 270.6 seconds in the control group at 12, 15 and 18 weeks, respectively. The mice exposed *in utero* spent a cumulative average of 207 seconds in the dark while the control mice spent an average of 234 seconds in the dark indicating decreased anxiety in the cellular phone exposed mice ($p < 0.001$) [Figure 1].

The Step Down Assay was performed on 98 mice at 12 weeks and in adulthood to determine fear of exploring the environment (51 control and 47 experimental mice). The test is performed by recording the time spent on a standard platform. A greater period of time on the platform indicates increased fearfulness. Exposed mice showed no significant difference in time spent on the platform when compared to the controls [Figure 1]. The control mice spent an average of 18.5 seconds while the experimental group spent an average of 16.7 seconds ($p = 0.59$) [Figure 1].

Overall, the mice exposed *in-utero* to radiation were hyperactive, had decreased memory, and decreased anxiety.

To understand the mechanisms underlying the changes in the memory and hyperactivity in animals exposed to radiation *in-utero*, we examined whether changes in the neuronal circuitry occurred in brain areas responsible for these compromised behaviors. Specifically, we asked whether changes in the synaptic transmission in CNS neurons are responsible for impaired memory and hyperactivity in radiation-exposed animals. The prefrontal cortex (PFC) is responsible for executive functions by screening distractions and maintaining attention in goal-oriented behaviors. Impairment of the PFC leads to dysregulated behavior/emotion such as ADHD¹⁶. The pyramidal neurons, the primary cell type in this structure, regulate attention and behavior through a complex and interconnected network. Whole cell patch clamp recordings of miniature excitatory postsynaptic currents (mEPSCs) were performed in pyramidal neurons of the PFC in control and cell phone-exposed mice. mEPSCs were generated by random vesicle release of glutamate from presynaptic neurons in the absence of stimulation. The measurement of mEPSCs is used to analyze the efficacy of synaptic transmission. Changes in mEPSC frequency are thought to result from modification of the presynaptic component of synaptic transmission, while amplitude changes indicate alterations in the postsynaptic component^{17,18}. Coronal prefrontal cortex slices (300 μ m) were prepared from 3–4 week old mice. mEPSCs were recorded in layer V pyramidal neurons in the prefrontal cortex in mice exposed to *in-utero* radiation for 9, 15 and 24 hours/day throughout gestation; the detection and analysis of mEPSC frequency and amplitude were performed as we described previously¹⁸. In animals exposed to *in-utero* radiation for 24 hours/day, a decrease in the frequency of mEPSCs was seen (control: 1.00 ± 0.12 Hz, $n = 40$; 24 hours/day: 0.72 ± 0.06 Hz, $n = 43$, $p < 0.05$, t test, Figure 2A and B). The cumulative probability curves for the amplitude of mEPSC events recorded from the *in utero* cell phone-exposed mice (24 hours/day) shifted

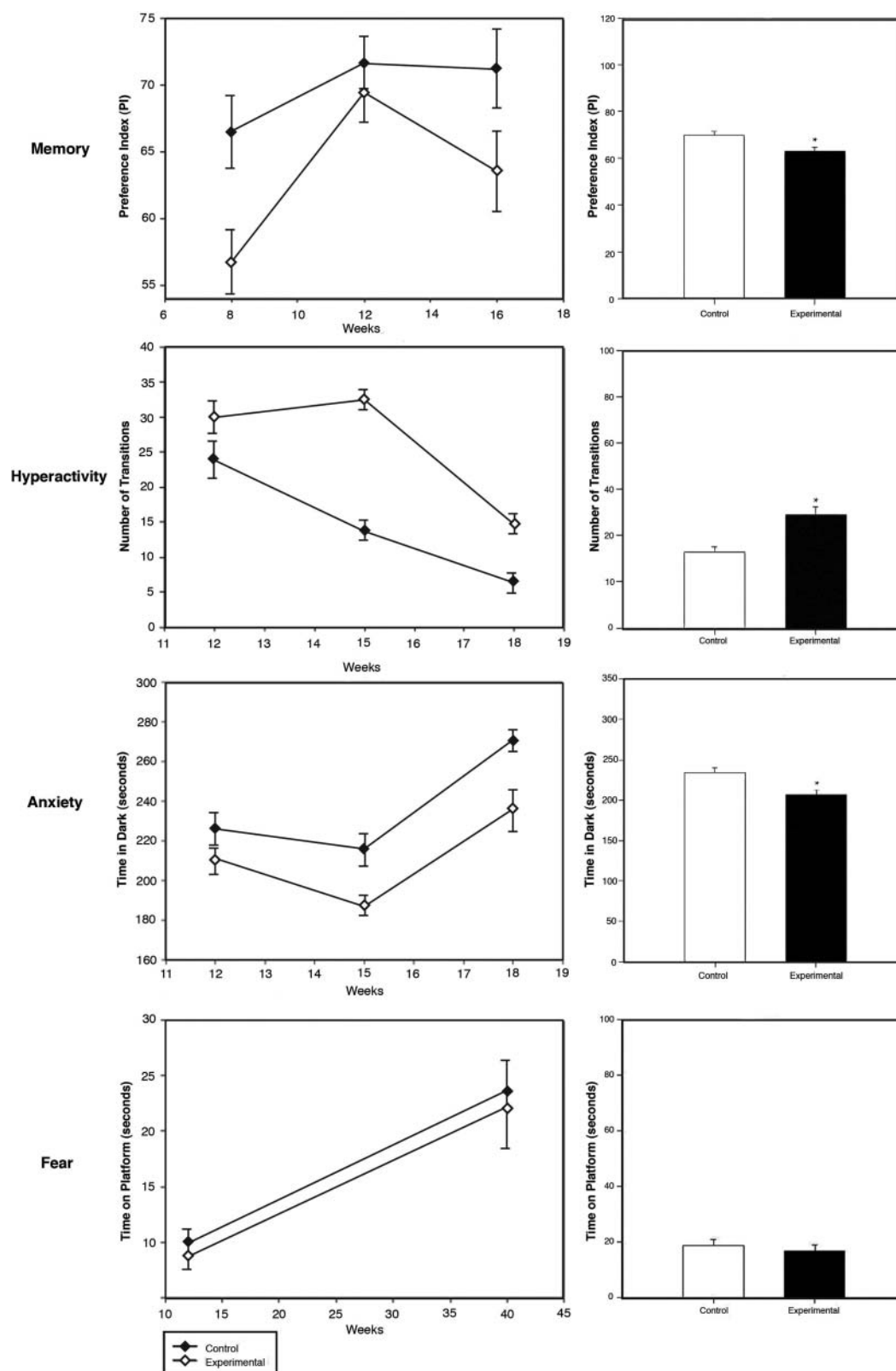


Figure 1 | Behavioral testing in exposed and control mice. The left column displays the data determined in mice at several ages after exposure. The right column demonstrates the cumulative average. To test memory the Standard object recognition memory test was used and a Preference Index (percent of total exploration time spent exploring the new object) shown at 8, 12, and 16 weeks of age. The cumulative mean preference index of the experimental group was 63.0% and the control group 69.9% (* $p = 0.003$, $n = 161$). To test hyperactivity we used the Light/Dark box test and display transitions at 12, 15, and 18 weeks of age. The cumulative mean number of transitions in the experimental group was 24.4 and the control group 16.4 (* $p < 0.001$, $n = 141$). To test anxiety we measured time spent in the dark at 12, 15, and 18 weeks of age. The cumulative average time spent in the dark in the experimental group was 207 seconds and in the control was 234 seconds (* $p < 0.001$, $n = 141$). To measure fear we used the Step down assay and display the time spent on the platform at 12 weeks and adulthood. The cumulative mean time spent on the platform in the experimental group was 16.7 seconds and in the control was 18.5 seconds ($p = 0.59$, $n = 98$).



significantly to the left relative to those recorded from the controls ($P < 0.01$, Kolmogorov-Smirnov test; control: 2765 events, cell phone exposure: 2224 events), indicating that the amplitude of mEPSCs was decreased [Figure 2C]. In a subset of experiments, we examined whether the reduction of mEPSC frequency depended on dosages of exposure in mice prenatally exposed 0, 9, 15 and 24 hours per day [Figure 3]. The trend of the dose-dependent decrease in the frequency of mEPSCs (0 hour/day: 1.37 ± 0.41 , $n = 9$; 9 hours/day: 1.27 ± 0.21 Hz, $n = 9$; 15 hours/day: 1.04 ± 0.20 Hz, $n = 10$; 24 hours/day: 0.72 ± 0.13 , $n = 11$) was statistically significant (linear correlation: Correlation Coef = -0.97 , Unadjusted $r^2 = 0.94$, $P < 0.05$).

Altogether, these results indicate that synaptic efficacy of glutamatergic transmission decreases at both pre- and postsynaptic sites in layer V pyramidal neurons. Thus, we demonstrate impairment in glutamatergic transmission (release from nerve terminals and glutamate receptor response) onto pyramidal neurons in the PFC after *in-utero* exposure to radiation from cellular telephones.

In a parallel experiment we examined whether *in-utero* radiation exposure led to changes in synaptic transmission in another brain area. mEPSCs were recorded in neurons in the ventral medial hypothalamus (VMH), a brain area implicated in the regulation of energy homeostasis^{19,20}. Our results indicated that in mice exposed to radiation for 24 hours/day, the frequency of mEPSCs (control:

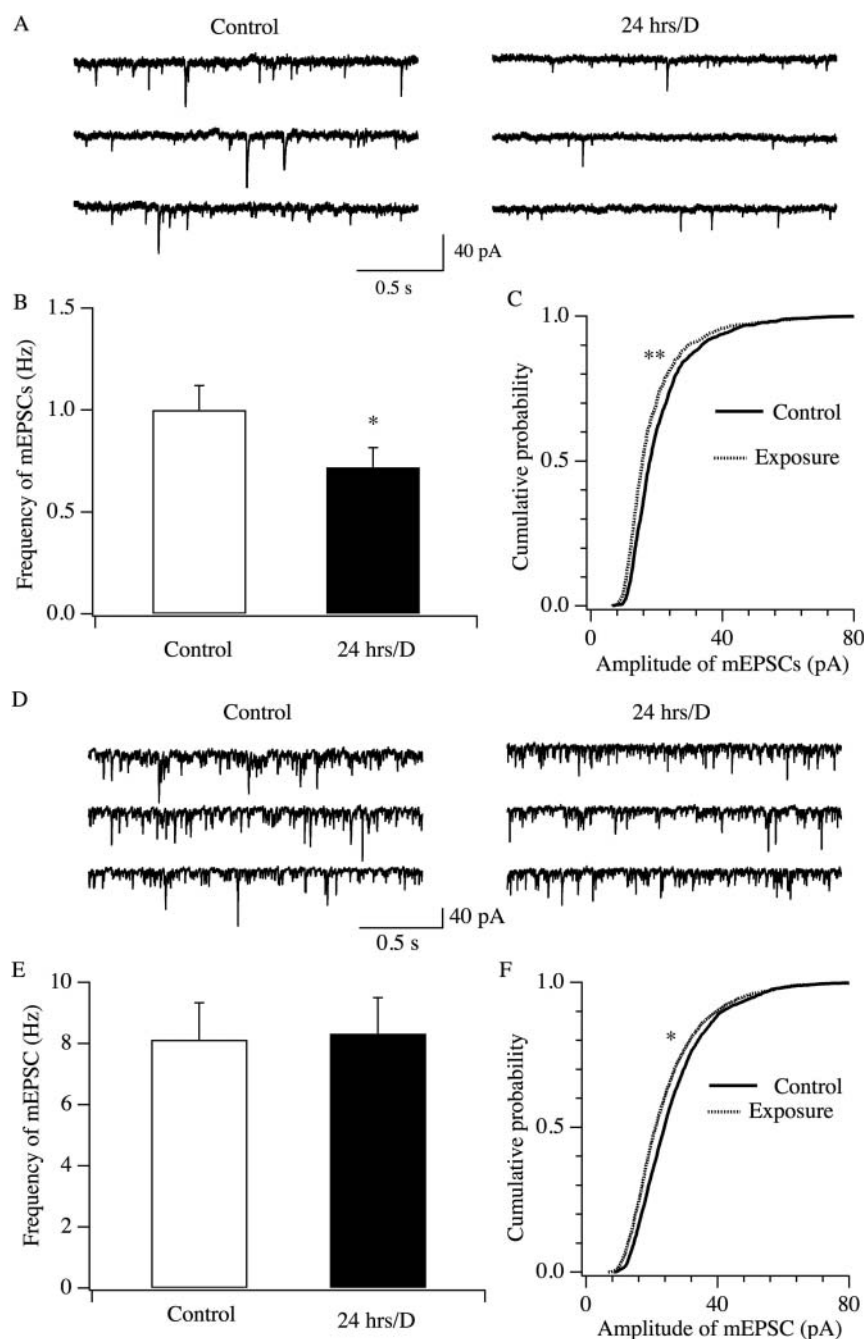


Figure 2 | Synaptic efficacy of glutamatergic synapses is decreased in brain neurons of mice after prenatal exposure to cell phone radiation. A–C, mEPSCs were recorded in layer V pyramidal neurons of the prefrontal cortex. Representative traces of mEPSCs from control and cell phone exposure groups are shown in A. mEPSC frequency and cumulative probability of mEPSC amplitude from both groups are shown in B (*, $P < 0.05$, t test) and C (**, $P < 0.01$, Kolmogorov-Smirnov test; controls, 2225 events; Exposed, 2766 events). D–F, representative traces, frequency and amplitude of mEPSCs recorded in neurons in the VMH are shown. *, $P < 0.05$, Kolmogorov-Smirnov test; Control: 2161 events, Cell phone group: 2261 events.

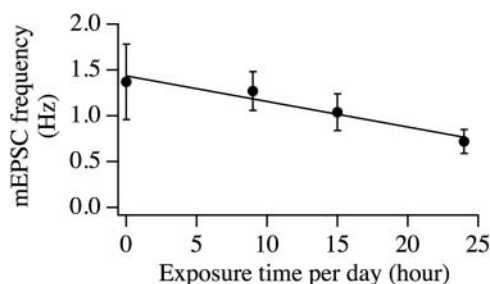


Figure 3 | A dose-dependent attenuation in the frequency of mEPSCs in layer V pyramidal neurons in mice. The frequency of mEPSCs recorded in mice prenatally exposed to cell phone radiation at of dose of 0, 9, 15 and 24 hrs per day are shown. Error bars are SEM. The dose responsive relationship is determined using regression analysis (Correlation coefficient, -0.97 ; r^2 , 0.94 ; $P < 0.05$).

8.13 ± 1.20 Hz, $n = 14$; cell phone radiation: 8.32 ± 1.17 Hz, $n = 14$) was not significantly different from that in control mice ($P > 0.05$, t test, Figure 2D and E). However, the cumulative probability of mEPSC amplitude recorded in radiation-exposed mice significantly shifted to the left ($P < 0.05$, Kolmogorov-Smirnov test; control: 2161 events, cell phone group: 2261 events; Figure 2F), suggesting that the amplitude of mEPSCs is smaller in the cell-phone exposed group than in controls. This result implies that an impairment of glutamatergic transmission occurs at the postsynaptic site. In summary, our results suggest that the effects of prenatal exposure to the cell phone radiation were not limited to the cortex.

Maternal stress can alter fetal development by increasing offspring exposure to corticosterone, causing cognitive deficits, hyperactivity, and alterations of the hypothalamo-pituitary-adrenal axis²¹. In order to exclude the possibility that impaired memory and behavior in exposed mice was caused by stress resulting from experimental manipulation, we measured serum corticosterone levels on day twelve of gestation using an ELISA assay. The mean corticosterone level in the exposed female mice (69.91 ng/ml, $n = 6$) was not significantly different from that in the control females (69.94 ng/ml, $n = 6$) [Figure 4], eliminating stress as a source of the observed behavioral and electrophysiologic differences.

Discussion

Here we demonstrate that fetal exposure to 800–1900 Mhz-rated radiofrequency radiation from cellular telephones leads to behavioral and neurophysiological alterations that persist into adulthood. Mice

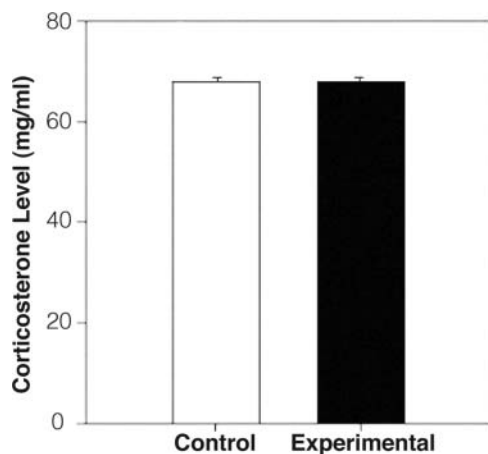


Figure 4 | Corticosterone levels during pregnancy were unaltered by exposure. The mean corticosterone level in the pregnant control females was 69.94 ng/ml and in the exposed female mice was 69.91 ng/ml.

exposed during pregnancy had impaired memory, were hyperactive, and had decreased anxiety, indicating that *in-utero* exposure to radiofrequency is a potential cause of neurobehavioral disorders. We further demonstrated impairment of glutamatergic synaptic transmission onto pyramidal cells in the prefrontal cortex associated with these behavioral changes, suggesting a mechanism by which *in-utero* cellular telephone radiation exposure may lead to the increased prevalence of neurobehavioral disorders.

This is the first study to specifically identify effects of radiofrequency exposure on the mouse fetus. During critical windows in neurogenesis the brain is susceptible to numerous environmental insults; common medically relevant exposures include ionizing radiation, alcohol, tobacco, drugs and stress. The effects of these agents are dependent on dose and timing of exposure. Even small exposures during periods of neurogenesis have a more profound effect than exposure as an adult. Alcohol affects cerebral neurogenesis, patterning of brain development and subsequent behavior. Maternal smoking also affects fetal development; fetal tobacco exposure results in a higher incidence of behavioral and cognitive impairment including ADHD. Similarly, prenatal exposure to cocaine can lead to behavioral disorders. Even prenatal maternal stress can lower intelligence and language abilities in offspring. As demonstrated by these examples, environmental exposures occurring in fetal life can lead to persistent neurological deficits. Exposure to these insults as an adult does not carry the same consequences. It is therefore not surprising that studies exposing adult animals to radiofrequency radiation failed to find similar significant defects in behavior. The exposure to cellular telephones in pregnancy may have a comparable effect on the fetus and similar implications for society as do exposures to other common neurodevelopmental toxicants. While this data demonstrates a clear association between fetal EMR exposure and neurodevelopment, it is important to recognize that the extrapolation of this animal model to humans is limited; the exposures used here are not identical to those experienced by the human fetus.

The molecular and cellular effects of radiofrequency exposure are not yet fully characterized. Multiple targets have been identified *in vitro*. Electromagnetic frequency exposure has been demonstrated to affect cell division and proliferation, both by inducing apoptosis and altering the cell cycle²². Electromagnetic radiation may promote the formation of reactive oxygen species (ROS) causing cell damage²³. One study specifically analyzing the effects of radiofrequency radiation on glioma cells demonstrated altered oxidative stress, a potential mediator of the alterations caused by electromagnetic radiation²⁴. Electromagnetic frequency radiation has also been found to activate ERK and p38 MAPK signaling²⁵. Although the precise molecular mechanisms that led to altered glutamatergic synaptic transmission in the prefrontal cortex identified in this study are not yet fully known, here we provide the first evidence that links changes in neuronal circuitry centered on layer V pyramidal neurons in the PFC with impaired memory and cognitive behaviors in animals exposed to radiation from cellular phone use. Our results indicate that the release of glutamate from the nerve terminals on PFC neurons and response of PFC neurons to glutamate are impaired in mice prenatally exposed to cell phone radiation. These results are consistent with previous reports that compromised glutamatergic transmission onto PFC neurons underlies impaired memory and cognitive functions in animals^{26,27}. Our results also imply that the effects of prenatal exposure to radiation on the brain might be global, since glutamatergic transmission onto neurons in another area of the brain (i.e., the VMH) was decreased as well. The effects of prenatal exposure to cell phone radiation may have more profound effects on brain functions than reported in this study. However, the effect was not identical; there are likely to be cell type specific or regional variations in susceptibility. Alternatively, the depth of the VMH may have shielded this region from maximal exposure.