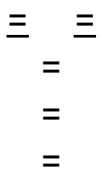
Radio-Frequency Electromagnetic Fields Produced By Wireless Technologies Might Actually Do Cause Adverse Health Effects



But how?

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ABSTRACT

There appears to be an increasing amount of scientific evidence showing that non-thermal radio-frequency electromagnetic fields emitted by wireless technologies can influence biological systems and can cause adverse health effects with prolonged exposure. However, a full understanding of the mechanisms behind these observed biological effects appears to not have been established yet. The lack of an established mechanism is one of the major culprits in the mainstream scientific debate on whether radio-frequency electromagnetic fields can cause adverse health effects. Studies showing biological effects are often dismissed on the basis that such effects are implausible according to current scientific understanding. Moreover, such claims are strengthened by an apparent lack of consistency in experimentally established effects. Therefore, our problem statement for this thesis is as followed: is it possible to form a plausible hypothesis of a coherent mechanism that is capable of explaining observed biological effects of radio-frequency electromagnetic fields from the current state of science in bioelectromagnetic research, epidemiology and associated fields? Our research methodology to answer this problem statement concists primarily of a review of scientific literature on research on biological mechanisms that might explain how biological systems can be influenced by electromagnetic fields. Some of the most promising hypotheses found in the scientific literature are relying on the frequently experimentally observed ability of radio-frequency electromagnetic fields to induce stress responses in biological systems. In the last part of our thesis, we extend upon the main potential mechanisms discussed, in order to show one consistent overarching mechanism can be hypothesized from current scientific insights to explain a variety of biological effects associated with radio-frequency electromagnetic fields. Seemingly inconsistent results that remain apparent even after considering methodological factors contributing to results, can be explained as the result of different outcomes of the same underlying mechanism. A careful treatment of available scientific literature on possible mechanisms that could explain observed biological effects of radio-frequency electromagnetic fields, suggests that the often made claim that inconsistent and seemingly contradictory results cancel each other out, is based on a lack of understanding of the possible mechanisms

involved. Based on our findings we may conclude that it is becoming increasingly necessary to reconsider the implications of long held scientific uncertainties about possible adverse health effects produced by non-thermal radio-frequency electromagnetic fields for society.

1. Introduction

In recent years an increasing amount of scientific studies point to observable adverse health effects produced by non-thermal, non-ionizing radiofrequency electromagnetic fields (RF-EMF[1]). However, at the same time a number of other studies seem to show conflicting results. These seemingly contradictory results, the difficulty in reproducing study results from different studies, and a lack of scientifically established mechanisms behind biological effects of RF-EMF, are often used as an arguments against the actual existence of adverse health effects related to exposure to RF-EMF.

However, a careful analysis of available scientific literature may reveal a different picture. In a previous paper we have discussed some of the causes of contradictory results in different studies on wireless phone use and brain tumor development (Frings, unpublished). Subtle differences in study design and analysis can explain seemingly contradictory results in a number of major studies on mobile phone use and brain tumor development. A more consistent picture, that appears to indicate more clearly the existence of adverse health effects associated with RF-EMF, arises when these subtle differences are taken into account. These observations give reasons for concern that an increasingly scientifically plausible view is establishing that suggests current widespread implementations of RF-EMF in modern wireless technologies can produce adverse health effects in biological systems.

Despite these advancements, it appears that there is still a need for a satisfactory model that fully addresses the possible biological mechanisms involved in these observed effects.

1 For this paper, whenever we use 'RF-EMF', we exclusively denote non-thermal forms of RF-EMF, except when otherwise noted.

There is a large amount of research done trying to uncover these mechanisms. Although great progress has been made in recent years, it appears that a number of observations remain unresolved up to this date. We believe these unresolved observations can be sufficiently explained when discoveries and observations from a number of scientific fields are taken into consideration. In this paper we will try to lay out the blueprints of notable scientific models that can explain the mechanisms behind observed biological effects arising from low level RF-EMF to a satisfactory level, based on current available scientific knowledge. The problem statement we will address in this paper will be: is it possible to form a plausible hypothesis of a coherent mechanism that is capable of explaining observed biological effects of RF-EMF, from the current state of science in bioelectromagnetic research, epidemiology and associated fields?

Given the possible major impact of a scientific acknowledgement of biological effects associated with exposure to RF-EMF within contemporary society, we will discuss the implications of these findings for the future of technology and society in the final part of this paper as well.

2. Short overview of Epidemiological studies

In our previous paper (Frings, unpublished) we mainly discussed two groups of epidemiological case-control studies that were influential for the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) to categorize RF-EMF as a possible carcinogen (group 2b) in 2011, next to one large cohort study that found no increases in brain tumor risk for mobile phone use. We will give a short summary of these studies in section 2.1 and 2.2. In section 2.3 we will give a short overview of more recent relevant epidemiological studies.

2.1. Case-control studies

Case-control studies are studies in which a group of subjects (the cases) exhibiting a condition or disease of interest, such as brain tumors, is compared with a group that lacks this condition (the controls). By comparing possible differences of behavior and other factors between cases and controls, a case-control study can offer insight into whether the manifestation of the condition of interest can be attributed to a specific factor, such as mobile phone use.

One major group of case-control studies in the past decade came from the international INTERPHONE group, and another group of studies came from the Swedish Hardell group. Together these two groups of case-control studies formed the primary studies for the IARC to classify RF-EMF as a possible carcinogen in 2011. Below we discuss these studies.

2.1.1. Hardell studies

The Hardell group did a number of carefully designed studies that found an increase in brain tumor incidence associated with high use of wireless phones, especially for high grade gliomas, the most common kind of brain tumors. The Hardell group assessed both combined and separate exposures to different types of wireless phones, including cordless phones and analog phones, and gives an overall consistent picture of increased brain tumor risk for high combined exposures and a high exposure to individual phone types. The most recent results from the Hardell group show up to a threefold increase in brain tumor risk with long time mobile phone use (OR (Odds Ratio) = 3.0, 95% CI (Confidence Interval) = 1.7–5.2 for gliomas in their >25 year latency group) (Hardell et al., 2015).

Although the Hardell group have produced consistent results with different studies throughout the years, their studies have been criticized by a number of researchers in the field. Most criticism is leveled at the inherent limitations of the case-control study design

and the use of exposure assessment based on memory recall of participants (Frings, unpublished). Despite these limitations, the Hardell studies have been considered the most reliable case-control studies published in this field to date (Lloyd Morgan, 2009; Davis et al., 2013).

Some researchers and reviewers have also pointed to apparent inconsistencies in the data of the Hardell studies, but, as discussed in Frings (unpublished), when carefully examined, these claims can be shown to be mostly unfounded.

2.1.2. INTERPHONE study

The international multi-center INTERPHONE study gave a far less consistent picture than the studies from the Hardell group. Regular use of mobile phones even showed significant decreases in brain tumor risks, for example OR = 0.81, 95% CI = 0.70–0.94 for gliomas, while only the highest category of cumulative use showed slight significant increased risk for brain tumors, OR = 1.40, 95% CI = 1.03–1.89 for gliomas (INTERPHONE Study Group, 2010). Given the unlikelihood of a protective role of RF-EMF for the development of brain tumors, the INTERPHONE report included an appendix in which the higher exposure groups where compared to the lowest exposure groups (instead of the control group). This showed more pronounced increases in risk for the development of brain tumors in the highest exposure categories (INTERPHONE Study Group, 2010). However, these results were not taken into the main conclusions.

Although larger in size than any previous case control study, the INTERPHONE study appears to suffer from number of issues besides the somewhat curious results, including a relatively low participation rate and less accurate exposure assessment than the studies from the Hardell group.

The participation rate is a calculation of the percentage of participants of a study (calculated seperately for cases and controls) compared to the total number of possible participants. A lower participation rate means a study has a greater chance of being affected by unknown selection bias. For example, heavy phone users might be too busy to reply to request to participate in a study, thereby skewing the data of heavy phone use in the assessed groups.

The biggest confounder in the exposure assessment of INTERPHONE is possibly the exclusion of cordless phone use. The role of cordless phones in epidemiological studies on mobile phone use and brain tumor risks is discussed in more detail in section 3.1.

Another main issue is that INTERPHONE used a more limited age range compared with the Hardell studies that, according to a reanalysis of the INTERPHONE data by the Hardell group, might have led to an underestimation of the risk (INTERPHONE Study Group, 2010, Hardell et al., 2011).

2.2. Cohort studies

The third major study discussed by us in Frings (unpublished) was the 2011 publication of the Danish Cohort Study that showed no association between mobile phone users and the general population of Denmark, putting doubt on the findings of the INTERPHONE and Hardell studies.

Cohort studies differ from case-control studies by taking a population group of interest, for example mobile phone users, to be followed and monitored for development of possible diseases, such as brain tumors, for a number of years. Incidence of disease in this group is then compared to another group, for example the overall population of a country. In principle cohort studies can yield more reliable results than case cohort studies, as it is

easier to monitor and collect precise data. This does not always translate into practice however, as can been seen when the Danish cohort study is examined more closely.

2.2.1. Danish Cohort study

The Danish cohort study is a population based study, whereby brain tumor incidence among a large set of (early) mobile phone subscription holders was compared to general brain tumor incidence in the rest of the Danish population. The study found no association between mobile phone use and brain tumor risks, but has been criticized for a number of major flaws in its study design. The biggest confounder in this study was the lack of adequate exposure data. The measurement of exposure was entirely based on the duration of subscriptions. No other measurements of exposure, such as total call time or number of calls, were used, making mobile phone usage data highly opaque. Additionally, the exposure group only included private phone subscriptions, as no personal data of business subscriptions was available that could be used for the study. This in turn meant that users of business subscribed mobile phones, potentially the heaviest user group, were excluded and left inside the general population of Denmark that formed the control group. Also no data of cordless phone use was used, nor was there data available about possible shared use of mobile phones by for example family members of subscription holders. (Frei et al., 2011, Söderqvist et al., 2012).

2.3. Other epidemiological studies in recent years

A number of other epidemiological studies have been published in recent years which we haven't discussed in Frings (unpublished), but it is worthwhile to summarize the most notable studies here for completeness.

One case-control study from 2011 among children showed some increase for the longest latency group, but there was no clear exposure-response relationship, and therefore the researchers concluded the data was not suggestive of any causal association. The lack of long term user data make these results uninformative however (Aydin et al., 2011).

A case-control study on acoustic neuroma (a rare kind of brain tumor that develops in the auditory vestibular nerve) was published by a research group associated with the Danish Cohort study, showing no increase in risk except for a non-significant increase for the most heavy use of cordless house phones (Pettersson et al., 2014). This study was commented on by the Hardell group for a number of concerns regarding the quality of the collected data (Hardell et al., 2014). Ironically, this study was later followed up by the research group, publishing an assessment of how exposure data from self-reported use measured up against exposure data taken from mobile phone providers (Petterson, 2015). They showed that self-reported use of subjects might be problematic for an accurate exposure assessment, arguing it could be a confounder for case-control studies in general. However, the Hardell group had already noted in their critique on this study that the time between tumor diagnosis and interviews of subjects was rather large, and that this would have affected memory recall (Hardell et al., 2014), indicating the quality of this study design was already sub-par compared to other case-control studies.

Another recent case-control study is the French CERENAT study, which found a significant increased risks (more than twofold increase) for meningioma and glioma brain tumors among the heaviest users of mobile phones (OR = 2.89, 95% CI = 1.41 – 5.93 for gliomas

and OR = 2.57, 95% CI = 1.02 – 6.44 for meningiomas), thus strengthening the results of the Hardell group and INTERPHONE studies that have shown an association between brain tumor risks and mobile phone use as well (Coureau et al., 2014).

2.4. Thyroid cancer

An additional recent publication by the Hardell group might be of interest, addressing an increase in incidence of thyroid cancer in Sweden and other Nordic countries in recent years that can be correlated with increased use of mobile phones (Carlberg et al., 2016). Carlberg et al. (2016) note these observations might be especially of relevance in light of new phone designs, where the antenna is placed on the bottom of the phone, leading to lower exposure for the brain, but potentially higher exposure to the neck.

It must be noted that a more recent publication by the IARC has linked observed increases in the incidence of thyroid cancer in different countries to over-diagnosis due to new diagnostic techniques (Vaccarella et al., 2016), though the data covered in this analysis only covers data up till 2007, while Carlberg et al. (2016) focussed on recent (more steep) increases, and postulate that improved diagnostic procedures can not entirely explain these reported increases.

3. On the importance of technicalities

The general view on research on possible adverse health effects associated with RF-EMF is that there is no consistent picture arising from available research results, and therefore there should be little reason for concern about the possibility that such effects actually exist. However, when published scientific studies are carefully examined, a different picture arises. In our previous paper we have shown that many seeming contradictions in results from different epidemiological studies can be largely explained by subtle differences in

study designs and faulty interpretation of technical specifications of wireless devices considered for inclusion in different studies (Frings, unpublished).

3.1. Example: cordless phones versus mobile phones

Several studies researching mobile phone and brain tumor risks leave out cordless house phones in their assessment, despite cordless phones using comparable technology for its wireless communication as mobile phones.

To understand why cordless house phones are generally not considered for inclusion in studies on mobile phone radiation and brain tumor risks, it is important to understand the difference between cordless house phones and mobile phones. Cordless house phones are landline phones that use wireless technologies comparable to those used in mobile phones. Since their introduction to the market in the early 90's, they have steadily replaced traditional corded phones in many households and offices. Both cordless phones and mobile phones work by sending and receiving RF-EMF signals to a 'base station' antenna. For mobile phones, these antennas are placed by mobile phone operator companies throughout most of urban and rural areas in the world. Cordless house phones do not communicate with mobile phone operator base station antennas, but connect to personally installed base stations that are directly connected to a landline connection within a household or office. Because they connect to personal base stations, cordless phones generally have a much smaller range of operation than mobile phones. Given their close proximity to base stations compared to mobile phones, it is generally reasoned that cordless house phones emit far less RF-EMF than mobile phones. A number of papers have noted however that the most common type of cordless house phones, DECT phones, emit comparable amounts of RF-EMF as mobile phones (Redmayne et al., 2010, Hardell et al., 2006). Some publications have negated these observations. However, as part of an assessment of different interpretations of research findings in Frings (unpublished) we have shown that a careful analysis of technical specifications of DECT phones and mobile phones and the amount of RF-EMF they emit, indeed shows DECT phones emit comparable

amounts of RF-EMF as mobile phones due to specific technical design choices. Taking into account the similarities between mobile phones and cordless phones, it can subsequently be expected that when DECT phones are not included in studies on mobile phone use and brain tumor development, and consequently instead DECT phone users are end up in control groups, exposure levels of RF-EMF might equal out between exposure groups and control groups, giving results that will seemingly contradict with studies that have adequately included DECT phone use in their exposure assessments (Hardell et al., 2011). The exclusion of DECT phones has nonetheless been a common practice in a number of major studies on mobile phone use and brain tumors. In combination with a number of other more or less compromising choices in study designs and assessments of results, as detailed further in Frings (unpublished), this might have led to unreliable research outcomes that have confused general public understanding of the current state of science in this field.

3.2. Developing understanding

Adequate assessment of the relevance of different published results is very difficult for the general public without a scientific background, leaving their scientific understanding in the hands of institutes that interpret and report on these findings in more simplified manners. Even for many people that do have a scientific background it can be difficult to interpret results of studies in this field however, as specific skills from a range of scientific disciplines are necessary to fully analyze and accurately interpret results in this field of research. This becomes especially apparent when looking into scientific publications of laboratory experiments with animals and in vitro cells, and even more so in publications on the possible biological mechanisms behind observed effects, given the complexity of the subject matter in these publications.

The most straightforward way to overcome the hurdles of complexity is by developing greater understanding. Therefore we will present an overview of the current state of science in relevant areas of research in the following sections, starting with animal studies.

4. Animal studies

Given the inherent limitations of epidemiological case-control studies discussed previously, these studies in themselves do not supply sufficient evidence for a causal association between RF-EMF exposure and increased cancer risks. Although cohort studies in principle should be able to give more reliable results, up to date no properly setup cohort studies have been published. Therefore for a general assessment of the possible carcinogenic effects of RF-EMF, it is necessary to also consider in vivo animal studies and in vitro studies on biological systems.

4.1. IARC monograph on animal studies

The IARC (International Agency for Research on Cancer) reviewed a wide range of animal and in vitro of studies in addition to considering the existing epidemiological evidence. Overall a mixed picture arises, with many studies seemingly contradicting each other, but nonetheless the IARC concluded that there is limited evidence of carcinogenic effects from animal and in vitro studies (IARC, 2013). To come to a proper assessment, the IARC took note of many factors that could contribute to apparently contradicting results. The IARC monograph lists a wide variety of possible confounders affecting research results, ranging from differences in biological effects of continuous and pulsed RF-EMF fields, the possible different effects of different kinds of polarization of RF-EMF used in different experiments, the influence of other EMF such as ELF (power grid) EMF, and differences between cell cultures and animal species. Some other factors leading to different results will be discussed in more detail next in section 4.2.

4.2. Health Council of the Netherlands assessment of animal studies

It should be emphasized the IARC monograph makes it clear that differences in study design besides size and statistical significance should not be ignored when comparing study results. Although this might seem to be a common sense remark from a scientific point of view, this capacity for common sense seems to be disturbingly absent in a number of review publications, such as the review of animal studies by the Health Council of the Netherlands (Health Council Of The Netherlands, 2014), released as the second part of their assessment on the possible carcinogenicity of RF-EMF. Although some attention is given to differences in setups, there is little discussion of how these differences might influence results.

It appears to be clear that of the 54 studies reviewed by The Council (as the 'Health Council of the Netherlands' will be referred to in this paper henceforth), most gave no results. However, with the lack of a thorough assessment of specifics of study designs, and the complete omission of studies on indirect mechanisms that could be associated with cancer development, it is little informative. Despite giving a far less thorough analysis, The Council manages to come to a different conclusion than the IARC did before in 2011, and, like in the first part of their assessment, conclude that overall, the evidence is not supportive of a link between RF-EMF and cancer. Therefore, according to The Council, there is no reason to adjust current regulations in the Netherlands, nor reason to consider precautionary measures. In light of the many errors we found in the first report of The Council (Frings, unpublished), we see little reason to trust these claims without careful scrutiny. Reassessing the entire second report of The Council unfortunately falls outside of the scope of this thesis. However, we will discuss one issue to illustrate why this report of The Council again requires a careful reanalysis before considering taking over its recommendations.

4.2.1. Restrained animal studies

There are a number of different experimental setups used in the past in animal studies. Two major different approaches can be distinguished which are relevant to compare. Most animal studies are done with either rats or mice. Due to specific factors, it has proven difficult to control exposure levels of RF-EMF in experiment setups. Either animals are allowed to roam free in their cages, and are exposed to RF-EMF of varying strengths in the entire cage, or animals are restrained in small tubes or comparable setups, in order to simulate human localized exposure to the head. Although in the latter case exposure can be controlled far more precisely, it brings a number of problems that free roaming setups do not have. Animals can only be exposed for a few hours a day in restrained setups, limiting the amount of exposure that can be simulated. Additionally, animals are refrained from maintaining their normal eating and sleeping cycles, which can influence metabolism and thereby the effect of possible toxic agents. Most importantly however, restraining of animals brings additional stress to the animals. Although most studies have used sham controls in order to compare results between exposure and non-exposure, increased stress levels might still influence detectability of biological effects induced by RF-EMF (Lerchl, 2009). Still, these studies make up a large proportion of the overall available animal studies on RF-EMF. If the stress experienced by the animals in these setups is indeed a confounder even when sham controls are used, this means that a substantial number of studies are of little value for an overall assessment.

Although The Council notes the use of restrains and lists 27 studies of the 54 studies assessed as using (partial or complete) restrains, it does not consider the potential influence of restrain stress on the possible outcomes. This is particularly of concern when The Council notes two replication studies that changed the experiment setup of a study being replicated, most notably, from a free roaming setup to a restrained animal setup. While the original study showed increased tumor risks, the replications studies failed to do so (Health Council of the Netherlands, 2014, p. 32).

In fact, none of the restrained animal studies show increased tumor rates according to The Councils analysis, while three restrain studies show decreased rates of tumors. Of the 26 studies using free roaming setups, 9 show increased tumor rates, while one free roaming study, which additionally injected the mice with tumor cells, showed decreased tumor rates after exposure to thermal levels (35 W/kg) of RF-EMF. One study of which the setup was unknown also showed increased tumor incidence.

It should be noted that five of the studies showing increased tumor rates were not considered for inclusion in the final appraisal of The Council, however, due to lack of sufficient study designs according to their analysis (one study showing inhibiting effects was also excluded, and one of the 40 studies showing no effects was deemed insufficient as well) (Health Council of the Netherlands, 2014, pp. 71-80).

4.2.2. Past remarks on future research

There is one interesting remark in the second report of The Council, which seems to have become especially relevant in light of recent developments. The Council gave off a negative advice for any further animal studies, based on the lack of consistent results in previous studies, and the fact that the publication of a large 25 million dollar animal study setup by the US government was underway. The results would be expected in 2016(Health Council of the Netherlands, 2014, p. 51).

Although publication of the final results of this study have since been delayed, preliminary results were released in the final week of May 2016 (while still awaiting peer review) (Wyde et al., 2016), but it appears these results came in too late for The Council to include in their third and final report released in the beginning of June 2016 (after several delays as well).

To the surprise of many researchers in the field, the US study, which used free roaming animals and carefully controlled exposure levels, appears to give clear evidence of carcinogenic effects in RF-EMF exposed rats, but the publication has been received with a large storm of critique, mainly within the mainstream media, fueling discussion about the findings and their relevance (Microwave News, June 10, 2016). However, within the research community the results had been widely anticipated from all sides, given the rigorous scale and design of the study, and the published preliminary results are regarded to be a possible game changer.

We will leave a full discussion of these results for when they are published in full. For now, there are still some interesting observations in the third and final report of The Council to consider.

5. Third report of the Health Council of the Netherlands

First of all, The Council, consisting of about 20 professors and experts at the time of publication, seemed very much set on keeping its quality control on par with its previous two publications on mobile phone radiation and cancer. Already in the introduction several errors can be noticed for the casual observer. Though insignificant for the content, it leaves one wondering how the report came to being over the course of several years of delay. In the first paragraph of the summary, it is mentioned the IARC classified RF-EMF as a possible carcinogen in 2012. In the introduction a few pages later, the date is magically shifted to 2010. (Health Council of the Netherlands, 2016, pp. 15-19). A curious thing, as the IARC classified RF-EMF as a possible carcinogen in May 2011, and released the full monograph detailing the categorization in 2013 (IARC, 2013).

5.1. On missing the relevance of promotion effects

There are more inconsistencies found on the first few pages of the report, but let's not get distracted by such trivial errors. In the summary The Council produces some more considerable contradictions, but these might easily slip the attention of the reader. It notes for example that a number of epidemiological studies show unexplainable increases in brain tumor risks already after short exposure (Health Council of the Netherlands, 2016, p. 16). These increases cannot be explained when considering the likely time it takes for tumors to develop, and therefore seem to impair the reliability of these studies. However, just a paragraph down The Council notes there are a few animal studies that have shown promotion effects of RF-EMF, accelerating the development of tumors initiated by other carcinogenic substances (Health Council of the Netherlands, 2016, p. 16). Although it is praiseworthy The Council has taken a more prominent note of these possible mechanisms, it is curious to say the least The Council appears to be oblivious to the fact that promotion effects can easily explain the early risk increases seen in some epidemiological studies they mention just a paragraph earlier, and that the role of promotion effects has been discussed by these epidemiological publications themselves (Hardell et al., 2013a, 2013d).

5.2. Recent brain tumor incidence.

The remaining parts of the 2016 report contains little new viewpoints on epidemiological findings. The Council has taken note of the increasing incidence of high grade gliomas found by Ho et al. (2014), but explains these as the result of new diagnostic techniques (after consulting Ho et al.). Furthermore it hasn’t changed its views on studies of the Hardell group, noting they still contain ‘inconsistencies’ (which however, as discussed in Frings (unpublished), mostly seem to be the result of their own misinterpretations). The only major difference in regards with the treatment of the Hardell studies, is that The Council now acknowledges these studies do not contain questionable response rates anymore (at

least in the most recent publications). See Frings (unpublished) for a treatment of this perceived issue as well.

5.3. New replication study on promotion effects

The observations of a possible tumor promotion effect is primarily reinforced by one new replication study published in 2015 (Lerchl et al., 2015). Despite comparable results as the study this replication was based on (Tillmann et al., 2010), The Council notes the lack of a clear exposure-response relationship, and therefore considers the findings of limited value for the overall assessment of the possible carcinogenicity of RF-EMF, and remains largely by its previous conclusions. It is a pity The Council did not take the time to consider the pre-publication of the major US animal study, as it would give basis for a more cautionary definition of the possible health risks of RF-EMF.

5.4. Consideration of studies on possible mechanisms

There is one more major weakness in the reports of The Council that requires attention, which is their refusal to consider studies on biological effects of RF-EMF exposure that indirectly could result in carcinogenesis. Given the difficulty of developing proper animal experiments specifically addressing long term, low level exposures to RF-EMF and its possible role in carcinogenesis (IARC, 2013), the inclusion of studies on biological mechanisms associated indirectly with carcinogenesis could have been informative for an overall assessment of the possible risks, especially in light of recent scientific results. Besides potentially serving as complementary evidence of studies showing direct carcinogenic effects, research into the mechanism behind carcinogenic effects of RF-EMF might also shed light on possible other adverse health effects of RF-EMF, and the possible overall role of EMF in biological systems.

6. Biological mechanisms

RF-EMF is considered a form of non-ionizing radiation. This means that RF-EMF do not contain enough energy to alter the electron configuration of atoms and molecules to the extent that they can become ionized. Following from this, RF-EMF should not be able to alter or damage organic molecules, such as DNA, directly, even at thermal exposure levels. The current established paradigm states that adverse health effects from exposure to RF-EMF can only arise when the strength of RF-EMF results in a substantial rise in temperature in an organic tissue that is exposed to these fields, resulting in damage due to the heating of tissue. This model in fact forms the reasoning for the current safety guidelines for the amount of RF-EMF that electronic devices can emit. According to these guidelines, RF-EMF are safe for as long as they do not result in a rise in temperature in exposed tissue of more than 1 degrees Celsius (ICNIRP, 1998).

However, many scientists engaged in bioelectromagnetic research and associated fields, have contested that these properties of RF-EMF exclude the possibility of biological interactions that could affect the functioning and well being of biological systems in other ways. This has formed the basis for a large amount of research in the field of bioelectromagnetics, with a wide range of different outcomes and interpretations of biological mechanisms associated with exposure to RF-EMF.

6.1. IARC monograph on biological mechanisms

The IARC monograph on RF-EMF covers an extensive amount of research on possible mechanisms that might support carcinogenic effects of RF-EMF. In this respect, although no conclusive evidence could be established, it appears one of the most considerable effects associated with RF-EMF exposure are oxidative stress and the production of reactive oxygen species (ROS) in biological systems. (IARC, 2013).

Although it is often argued RF-EMF do not have enough energy to destroy molecular bonds, processes of biological systems are far more sensitive to subtle changes in their environment. Thus far less energies might be required to affect processes in biological systems compared to non-living systems. There is still some debate going on about the extent to which RF-EMF can be “picked up” by biological systems to influence for example oxidative mechanisms, given the prevalence of thermal noise in these systems that should theoretically predominate over current exposure to RF-EMF (IARC 2013).

6.2. Possible role of oxidative mechanism in biological effects

However, the feasibility of oxidative mechanisms being influenced by RF-EMF has been reinforced by an extensive review published in 2015 which assessed 100 available studies on oxidative effects in biological systems exposed to RF-EMF. According to this review, 93 of the 100 studies showed significant effects (Yakymenko et al., 2015). Besides giving a plausible mechanism in which RF-EMF can indirectly lead to the development of cancer, Yakymenko et al. point out that a role of RF-EMF in oxidative mechanisms can not only explain observed carcinogenic effects of RF-EMf, but also a wide range of other effects that have been associated with RF-EMF exposure. Oxidative mechanisms play an important role in many different biological processes such as immune response, cellular communication and aging (Yakymenko et al., 2015).

6.3. Reactive Oxygen Species

In order to understand how RF-EMF can possibly influence oxidative mechanisms, it is important to understand what these mechanism exactly are. Reactive Oxygen Species (ROS) play a critical role in oxidative mechanisms in biological systems. ROS are reactive molecules containing one or more oxygen elements. The most common ROS is superoxide, a negatively charged oxygen molecule that is relatively reactive, and often forms more

complex ROS such as peroxide, hydroxyl radicals and singlet oxygen through these reactions. ROS play an important role in different cell processes, and are a byproduct of different mechanisms in cells where oxygen plays a role. However, due to the reactive nature of ROS, an overabundance of ROS in the cell can lead to cell damage, as ROS easily react with other molecules they come across, damaging these molecules in the process. Highly reactive ROS such as hydroxyl can for example in this way break DNA bonds when crossing DNA molecules, and can even cause chain reactions when reacting with certain cell structures such as lipids in cell membranes (Devasagayam et al., 2004; Turrens 2003).

6.4. ROS production

Yakymenko et al. (2015) note two main processes of ROS production which studies have shown are possibly influenced by RF-EMF. One is the process of NADH oxidase in cellular membrane, as suggested by Friedman et al. (2007). NADH oxidase can release large amounts of ROS as an immune system response. However, NADH also release ROS under different interactions, and RF-EMF might be able to modulate ROS production (Yakymenko et al., 2015; Friedman et al. 2007). The other mechanism of interest is the generation of ROS as a byproduct of adenosine triphosphate (ATP) production in mitochondria. In order to understand how these processes can be influenced, we will take a deeper look into ROS generation inside mitochondria.

ATP is a prominent energy transfer molecule produced by the mitochondria. ATP molecules are produced in a sequence of complex proteins which are part of a folded structure found inside mitochondria known as the Electron Transport Chain (ETC). In the ETC, oxygen is transported and at the end of the transport chain combined with an electron and two protons in order to form water molecules. However, sometimes the oxygen is prematurely released as a superoxide molecule, which can subsequently react with other molecules and form other, more reactive ROS that can cause damage inside the cell. About 1–2% of the oxygen molecules processed are prematurely released as superoxide. When biological

systems are exposed to RF-EMF, it has been hypothesized by Burlaka et al. (2013) this might contribute to increased release of superoxide from mitochondria by disturbing the process of the ETP to form water molecules.

It must be noted that biological cells are not defenseless against overproduction of superoxide, and have built in protection mechanisms such as in the form of the superoxide dismutase enzyme that can convert superoxide into less harmful chemicals (Turrens, 2003). Therefore biological systems can respond to reduce possible harm caused by potential damaging agents.

Given ROS play an important role in immune system response and cell communication, as noted above, the possibility that RF-EMF can alter ROS production can form the basis of a solid hypothesis as to why RF-EMF can lead to a multitude of effects related to immune system responses.

6.5. How ROS production might be influenced by RF-EMF

How RF-EMF can influence ROS production exactly remains yet unclear, so there are a number of possible explanations. One simple explanation might be that oxygen becomes more difficult to handle for processing chains inside the cell, due to increasing twisting movements of these molecules induced by RF-EMF, even before these induced movements lead to observable thermal vibrations. Furthermore, it has been suggested RF-EMF could alter the transportation of electrons in the processes described here. Such interactions would also be able to influence the reproduction of DNA molecules and other cell processes (Yakymenko et al., 2015), which might in turn lead to DNA damage. Although these possible mechanisms might be sufficient to explain the increased production of ROS and oxidative stress induced by RF-EMF in biological systems, other mechanisms might be at play as well. These could become especially relevant when considering more subtle, often dismissed but repeatedly observed contradictory (sometimes even seemingly beneficial) effects of RF-

EMF on biological systems, that primarily seem occur at short, (extremely) low exposure to RF-EMF (Yakymenko et al. 2015, Barnes et al. 2016).

In relation to these observations, we probably should make clear these seemingly contradictory effects in oxidative mechanisms for certain kinds of very low exposures to RF-EMF, should not too eagerly be compared directly with some of the apparent 'protective' effects observed in some epidemiological studies like INTERPHONE, as these observed effects are still more likely the result of research bias, given the many issues in these studies (as discussed in section 2.1.2 and section 3.1 and elsewhere). However, even the Hardell group observed some odd reduced risks in some of their meticulously set up studies — most notably a survival benefit for some heavy mobile phone users who developed low grade gliomas (in contrast with decreased survival rates for cases with high grade gliomas with heavy phone use). The Hardell group considers earlier detection of tumors, induced by symptoms enhanced by RF-EMF exposure, as the most likely cause for these survival benefits though (Hardell et al., 2013a).

6.6. Quantum mechanical interactions

As noted above, it is commonly noted that RF-EMF does not have enough energy to break molecular bonds, and therefore it should not be able to damage cell structures and molecules such as DNA directly. However, the fact that RF-EMF does not have enough energy to cause such damage, does not mean that it might not influence processes in other ways. Perhaps one of the most important observations to be made in this respect is that quantum mechanical interactions are less rigid than is most often presented. In the study of quantum physics, particle interactions such as photon absorption and emissions are devised according to the probability of their occurrence. Therefore what is often presented as a rigid interaction within quantum mechanics, sometimes exhibit anomalies. These are however generally dismissed in favor of frequently observed behavior in order to devise principle rules of interaction and transition. These rules are known as selection rules.

Transitions not following selection rules do take place, but at a much lower probability rate than those following selection rules. These uncommon transitions are known as ‘forbidden mechanisms’ or ‘forbidden transitions’ in spectroscopy (Selection Rule, n.d., Bunker et al., 2006). Interestingly however, such anomalies are responsible for certain well known phenomena such as phosphorescence, where the emission of absorbed photons in specific material is delayed and leads to an observed glow for a prolonged period after exposure to light. These are well established phenomena that seem to have little to do with biological effects of RF-EMF, but there are indication that in biological systems comparable but more delicate interactions might play a role.

6.7. Bioelectromagnetic interactions

Why such interactions might play a role in biological processes might be further illuminated when diving deeper into the field of bioloelectromagnetics. Many complex interactions based on different forms of EMF have been established in bioelectromagnetic research (Cifra et al., 2011). Some of these will be discussed later, but one curious subfield of bioelectromagnetics is the research into ultra weak photon emissions, or ‘biophotons’. Biophotons are photons emitted by common biological cells. The emissions are generally considered as side effects of oxygen reactions, as oxygen reactions produce photon emissions themselves, and are seen as a byproduct of normal cell metabolism and apoptosis. However, some researchers have begun to suggest biophotons play a crucial role in cell communication (Daviss, 2002). Cifra et al. (2011) note the ability of biological systems to delay photon emission in a non-linear fashion up to days after excitation. Furthermore, a number of studies have demonstrated the effect of biophotons on cell proliferation and other biological processes (Cifra et al., 2011, Popp 2003).

What is of special interest in the context of RF-EMF effects, is that biophotons appear to exhibit patterns of regulated emission, and cells even appear sensitive to minimal alterations in biophoton emissions (Cifra et al., 2011). Interestingly, cancer cells show more

active, but less regular emissions of biophotons (Hyland, 2009). This might indicate disrupted biophoton emission could play a role in cell communication and metabolism. Popp is one of the most prominent researchers in the field of biophoton emission, and has elaborated extensively on the possible role of biophotons in cell development and communication and research in this field showing such effects (Popp, 2003).

6.8. Distortions of immune system response

Living biological systems exist in a far more delicate balance than (basic) chemical molecules and atoms. It might therefore not be unreasonable to assume biological systems are far more susceptible to subtle electromagnetic changes in the environment. This notion can be supported by the wide range of available research showing oxidative effects from RF-EMF in biological systems (Yakymenko et al., 2015). Following from the available scientific research (Yakymenko et al., 2015, Cifra et al. 2011, Barnes et al. 2016), we believe it is possible to develop a hypothesis for a plausible mechanism of RF-EMF interactions with biological systems, in which observed effects might be further theoretically established if research can show RF-EMF can have a direct influence on biophoton emissions. Primarily, we suspect RF-EMF can influence biophoton emissions of biological systems, both through increased production of ROS but also by directly influencing biophoton emission due to stimulated fluctuations of EMF inside cells. If such an effect can be shown, different, often subtle, and sometimes seemingly contradictory effects of RF-EMF on biological systems can be explained in one mechanism of interaction.

If biophotons indeed play an important role in cell communication, regulating cell processes and immune system responses on an intercellular level, external factors that influence biophoton emissions could negatively influence important regulating functions in biological systems.

For example, when biophotons play a fundamental role in the ability to activate immune system response across multiple cells to counter invading organisms and abnormal cell proliferation, RF-EMF could potentially disturb these processes by changing the rate of biophoton emissions through subtle alterations of the EMF inside the cell. Such alterations could lead to enhanced biophoton emissions, which could initially trigger overreactions of the immune system across biological systems. Such activation of the immune system for a short duration can improve the cells defense, as it will be induced to react to possible damaging agents already present in the cell. However, for long periods of durations, enhanced photon emission inside the cell might result in less efficient response mechanisms to threats inside and outside of the cell, as the cell become depleted of 'stored' photons, reducing the ability for cells to emit biophotons and thereby impairing communication channels inside and in between cells.

In this way, RF-EMF could lead to distortions of immune system response mechanisms inside biological systems. Initially such reactions might not do much harm, as biological systems might activate their own counter mechanisms, but if prolonged exposures to RF-EMF take place, this might lead to an overexcited immune system with associated symptoms. In the long run this could even result in exhaustion of immune system response mechanisms. This in turn might make real threats, such as known carcinogenic agents, more hazardous. The immune system becomes less capable of responding adequately to the new threat, and in return the threat can wreak more damage.

6.9 Summary and recommendations on biological mechanisms

We must emphasize the specifics of the discussed biological mechanisms associated with RF-EMF exposure are still of speculative nature, but a thorough examination of the wide range of available scientific literature in the field of bioelectromagnetism and associated fields should leave little doubt that research in these fields is far more developed than skeptics of RF-EMF effects often suggest.

If research efforts are increased to further explore these kinds of biological mechanisms, this should lead to greater insight on the possible mechanisms behind repeatedly observed carcinogenic effects of RF-EMF in epidemiological research and carefully devised animal studies.

Most importantly however, taking into consideration complex processes taking place inside biological systems and the influences of RF-EMF on these processes, can explain many different observed effects of RF-EMF which often seem unrelated or might even appear contradictory, such as diseases associated with autoimmune responses. These effects might arise in subjects whose immune system would get in a heightened state of activity from exposure to RF-EMF. Similarly, pathologies associated with a dysfunctional immune system such as cancer can be expected to arise after prolonged exhaustion of the immune system and associated processes. In this respect, especially for future animal studies it should be worthwhile to do a parallel analysis of different pathologies, in order to see wether there is a (possibly inverse) relationship between carcinogenic effects and for example autoimmune pathologies.

7. Concerns for society

In light of scientific developments surrounding RF-EMF health research discussed above, it seems foolish for society as a whole to not take a more precautionary stance towards the implementation and use of RF-EMF technologies. As discussed in Frings (unpublished), a number of countries such as France, Belgium and Italy have already implemented precautionary measures based on the current state of science, advising the public to limit exposure, and sometimes even restricting the sales of wireless devises aimed at children.

A careful analysis of research into mechanisms behind potential adverse health effects seems to give only more reason to take the potential health risks of RF-EMF serious. A

definite answer will not come any time soon though, due to the nature of scientific research in general taking years to complete, and reaching a general consensus among scientists on mechanisms of action and interpretation of different research results can easily take up decades. If, by then, it becomes established that RF-EMF do cause adverse health effects, given the current widespread and continuously increasing implementation of RF-EMF in society, a scientific consensus will come too late for many people already affected by exposure to harmful levels of RF-EMF.

Therefore, we believe society should not wait for the scientific community to resolve issues of uncertainty on potential adverse health effects of new technologies. Instead, we believe society should seek to answer the question how to deal with inherent uncertainties new upcoming technologies such as RF-EMF technologies bring with them as they are being introduced to society.

7.1 Acknowledging uncertainty

How do we, as a society, handle the uncertainties of new technologies and substances? A brief look at the history of industrial technological development shows we have been here many times before (Michaels, 2008), and often it did not end well when no proper precautionary measures were taken. However, it is possible to change our attitude and not repeat such mistakes indefinitely with every new development introduced by science and technology.

We believe the simple solution to such grave errors of the past and present, is people should be adequately informed about the uncertainties which developments in science and technology bring, so that people can decide for themselves what risks they are willing to take.

In the case of RF-EMF and health, the rising amount of research showing biological effects of RF-EMF are an indication people should be advised to limit the use of wireless technologies. Although there is no definite answer yet on the question whether RF-EMF can indeed be harmful, there is no rationalization for not letting people for themselves decide to reduce their exposure until sufficient scientific insights have been established

We believe that in a reasonable society this should be the norm for any new technology. There is no need to rush developments. Society as a whole would benefit instead if the pace of adaptation was distributed over individuals by the extent to which they are willing to consciously accept the risks involved with the adaptation of new technologies. Pioneers can lead the way and take the bigger risks to the extent they feel comfortable with, while the general population can follow on their own terms.

Currently however, people in a number of countries such as the Netherlands, UK and USA are shown a false image of the level of safety and certitude, and are misled into following technological trends that in reality require a great amount of reservation for most. Those who are more vulnerable to the risks, such as children, people with frail health and people planning on starting a family, are now thrown into a gamble of scientific uncertainties, seemingly primarily in order to maintain corporate profits and personal gains of the elite that dominate technological and economic developments in society. A bleak reality that has to be confronted by those that do not want to end up at the wrong side of the equation. We have to leave a detailed treatment of these subjects for another time though.

8. Conclusion

The most important observation that should arise from this treatment of available scientific literature on possible interactions of RF-EMF and biological systems, is that, despite common believe, research in this field is anything but settled. An increasing body of scientific research

shows there is reasonable amount of evidence to support the hypothesis that non-thermal RF-EMF can cause substantial adverse health effects. Taking into account mechanisms behind RF-EMF health effects based on stress responses, we have sketched a plausible hypothesis to show that the currently available scientific research and insight can be developed further to support a single coherent model of interaction that can explain a number of seemingly unrelated effects observed in a wide range of research on RF-EMF health effects. In this way, we have tried to show that a careful treatment of available scientific literature on possible mechanisms of observed biological effects of radio-frequency electromagnetic fields, can counter the often made claim that inconsistent and seemingly contradictory results cancel each other out. In short, such claims are based on a lack of understanding of the possible mechanisms involved.

There is still enough room for debate, and more research is inevitably necessary to get a comprehensive view on what is exactly going on in this field of science. However, even with the most well designed studies, it is unlikely we will get a definitive answer within the coming years to the question whether RF-EMF indeed cause adverse health effects. Any well devised study will require years to complete, and exact replication studies would be additionally needed before establishing long term biological effects as pretty certain, while scientific consensus might take even decades to establish.

Based on our findings, we may conclude that for society it is becoming increasingly necessary to reconsider the implications of long held scientific uncertainties about possible adverse health effects produced by RF-EMF. In light of the possible implications of a widely used technology such as RF-EMF influencing health in a number of ways by affecting the general functioning of the immune system in biological systems, potential carcinogenic effects of RF-EMF should furthermore not be the only health concern to be addressed in future scientific research. Other health issues such as auto-immune diseases should be carefully researched as well in relation to RF-EMF exposure.

Given the current state of science, we believe early warning signs should be taken seriously for as long as there still is substantial scientific uncertainty in this field of research. Precautionary measures should be implemented imminently by societies using RF-EMF technologies for as far as they have not yet done so, to limit and prevent the manifestation of possible undesirable health effects among the general public for as much as possible.

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