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

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

Wireless mobile phone communication is globally ubiquitous and popular. There have long been concerns regarding possible adverse biologically-related health effects of exposure to radiofrequency electromagnetic field (RF-EMF). The central nervous system (CNS) is a main concern with regards to the effects of RF-EMF, since mobile phone use involves close exposure or immediate contact with the head[1]. The biological effects of RF-EMF exposure on human health remain unclear because of conflicting findings of various studies[2,3].

A number of studies have reported that RF-EMF exposure of animal models increases blood-brain barrier permeability, impairs intracellular calcium homeostasis, alters neurotransmitters, and increases neuronal loss and damage in brain tissue[4–8]. Epidemiologic studies have linked RF-EMF exposure from mobile phones with neurological and cognitive dysfunctions[9–11].

Cellular effects of RF-EMF exposure reportedly involve the apoptotic pathway, extracellular signal pathway, DNA damage response, cell proliferation, and cell cycle[3,12–15]. The effect of EMF exposure on autophagy in mammalian cells has been documented[16,17]. Autophagy is catabolic cellular degradation process responsible for degrading damaged organelles or unusual protein aggregates, which is activated in the presence of a variety of stimuli[18]. Suppression of autophagy may have a role in progression of cancers, neurodegenerative diseases, and infections, and is a common feature of aging[19,20]. Therefore, autophagy plays an important role in maintaining cellular homeostasis and further functions protecting cells from various stressors[21].

The cerebral cortex is a thin layer of neural tissue[22] that surrounds brain tissues such as hippocampus, striatum, basal ganglia, and thalamus. In addition, the mouse cortex has a smooth surface, while that of humans is folder rather like a walnut[23]. It is a highly-developed region of the human brain that processes most of the actual information, including sensory functions, such as hearing, touch, vision, smell, and movement, as well as cognitive functions, such as thought, perception, memory-related problem solving, and understanding language[24,25].

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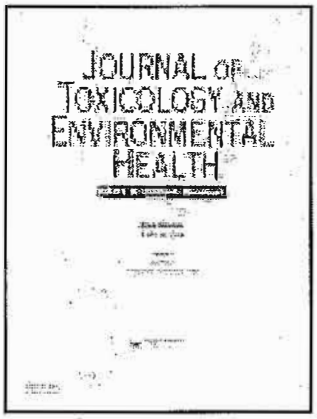

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Could Myelin Damage From Radiofrequency Electromagnetic Field Exposure Help Explain the Functional Impairment Electrohypersensitivity? A Review of the Evidence

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COULD MYELIN DAMAGE FROM RADIOFREQUENCY ELECTROMAGNETIC FIELD EXPOSURE HELP EXPLAIN THE FUNCTIONAL IMPAIRMENT ELECTROHYPERSENSITIVITY? A REVIEW OF THE EVIDENCE

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Myelin provides the electrical insulation for the central and peripheral nervous system and develops rapidly in the first years of life, but continues into mid-life or later. Myelin integrity is vital to healthy nervous system development and functioning. This review outlines the development of myelin through life, and then considers the evidence for an association between myelin integrity and exposure to low-intensity radiofrequency electromagnetic fields (RF-EMFs) typical in the modern world. In RF-EMF peer-reviewed literature examining relevant impacts such as myelin sheath, multiple sclerosis, and other myelin-related diseases, cellular examination was included. There are surprisingly little data available in each area, but considered together a picture begins to emerge in RF-EMF-exposed cases: (1) significant morphological lesions in the myelin sheath of rats; (2) a greater risk of multiple sclerosis in a study subgroup; (3) effects in proteins related to myelin production; and (4) physical symptoms in individuals with functional impairment electrohypersensitivity, many of which are the same as if myelin were affected by RF-EMF exposure, giving rise to symptoms of demyelination. In the latter, there are exceptions; headache is common only in electrohypersensitivity, while ataxia is typical of demyelination but infrequently found in the former group. Overall, evidence from in vivo and in vitro and epidemiological studies suggests an association between RF-EMF exposure and either myelin deterioration or a direct impact on neuronal conduction, which may account for many electrohypersensitivity symptoms. The most vulnerable are likely to be those in utero through to at least mid-teen years, as well as ill and elderly individuals.

A recent report by the Health Council of the Netherlands highlighted the importance of myelination because of its role in providing electrical insulation to the nerve fibers (Health Council of the Netherlands, 2011). The council raised an important question: Can exposure to external electromagnetic fields, which create an electrical field in the brain, affect natural development and pruning of synapses during human development? This conservative advisory body stated that it is of "great importance to gather more information on this" (20). The council refers to both radiofrequency and extremely low-frequency electromagnetic field (RF-EMF and ELF-EMF) exposures at intensities too low to produce thermal damage. These are omnipresent, both environmentally (such as from mobile phone base stations and WiFi routers) and individually (such as from mobile phones, tablets, laptops, and iPods). The council's question is relevant and particularly important in the unborn and very young. The

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brain develops rapidly in utero, and at critical stages of development from infancy through adolescence and early adulthood, when axons and dendrites undergo pruning and synapses are formed. The process occurs under the influence of the brain's internally generated electrical activity in concert with an intricate chemical crosstalk using growth and differentiating factors as well as modulators and co-modulators (Fuxe et al., 1986).

Individuals claiming to suffer from exposure to electromagnetic fields (EMF) have been reported. In Sweden, electrohypersensitivity (EHS) is an officially fully recognized functional impairment (i.e., it is not regarded as a disease). Those who are electrosensitive commonly indicate having particular sources of exposures to which they are sensitive, which vary among those with the condition (Röösli et al., 2004). A rudimentary analysis comparing reported symptoms of those having EHS with those in a Swiss Health Survey showed significantly increased incidence of sleep disorders and severe headaches, and a reduced incidence of asthma in those with EHS (Röösli et al., 2004). With repeated exposures, response time reduces and reaction tends to grow more severe than when symptoms from the same source were first experienced, unless there has been an unexposed period of months, after which recurrence of symptoms may take a day or more (personal communication, Rob Hutchins, spokesperson for ElectroSensitivity New Zealand, April 2014).

Different sources may elicit different responses in any one person. Röösli et al. (2004) noted a trend toward more headaches in those using (cathode ray) display terminals, concentration problems and tinnitus with use of communication devices (RF), and nervousness or distress from ELF exposures. This is in agreement with the findings of Gordon et al. (1963), who suggested that "with low-intensity irradiations [1 mW/cm^2], the degree and sometimes even the nature of the functional and morphological changes depended on the wavelength." It may also explain why double-blind exposure studies with electrohypersensitives and a control group have not generally or consistently found a significant relationship (Rubin et al., 2005), as responses appear not to be uniform (Havas, 2013) and depend upon the stage of EHS and the time since the last exposure.

In Sweden, the prevalence of EHS was first estimated at 1.5% of the population in a survey undertaken in 1997 (Hillert et al., 2002), and a newer estimate is 2.6–3.2% (Johansson, 2006). In Austria the prevalence was estimated to be less than 2% in 1994 but rose to 3.5% in 2001 (Schrottner and Leitgeb, 2008). In California, the prevalence of self-reported sensitivity to electromagnetic fields was 3.2%, with 24.4% of those surveyed also reporting sensitivity to chemicals (Levallois et al., 2002). In Switzerland, 5% of the population was estimated to suffer from EHS in a survey undertaken in 2004 (Schreier et al., 2006). Finally, the Canadian Human Rights Commission noted that approximately 3% of Canadians have been diagnosed with environmental sensitivities, including to chemicals and EMF in their environment (Sears, 2007). In the report, Sears (2007) recommended improving the environmental quality at workplaces.

In yet unpublished studies by Johansson et al. (personal communication), the epidermal nerve fibers of electrohypersensitive persons were markedly reduced in length and number of nerve terminals, indicating apparent damage. The question is whether this occurred due to myelin sheath destruction or functional axonal conduction disruption. In neuroscience it is a well-established fact that reduction of the number of nerve fibers and concomitantly axonal terminals leads to an elevation in sensitivity, the so-called supersensitivity phenomenon (Gerfen, 2003). Can these also be underlying mechanisms for electrohypersensitivity?

This review focuses on effects attributed to RF-EMF. Extremely low-frequency (ELF) effects are also important to explore with relation to myelin, as there have been studies conducted regarding the use of ELF for therapeutic purposes (Sherafat et al., 2012; Baptista et al., 2009; Protasoni et al., 2009; Aydin et al., 2006; Mert et al., 2006). Perhaps the most important observation regarding these is that they present vital evidence that biological effects are

frequency dependent: that is, responses may be positive, neutral, or negative, depending upon the frequency of the exposure. However, the associations of ELF and myelin integrity were not examined.

It is also pertinent to ask whether nonmyelinated nerves are more susceptible to direct interference from RF EMF, but this also lies outside the scope of this article. Briefly, there are studies that demonstrated redistribution of transmembrane sodium channels after exposure to pulsed RF EMF (Schneider and Pekker, 2013), and changes in neuronal firing rate and plasma membrane properties after extremely low, brief exposures of neonatal rat cerebral cortical tissue (Pikov et al., 2010).

In this review, we examined whether there may be a connection between symptoms reported after exposure to RF-EMF (chronic and acute nonthermal exposures) and compromised myelin integrity. Is there any evidence to suggest it, and is the hypothesis reasonable? These are important questions because loss of myelin is critical in several diseases, including multiple sclerosis (MS).

The aim of this review is to outline what myelin is and its normal course of development over the life span. Animal studies examining effects of RF-EMF on myelin sheathing and epidemiological research examining multiple sclerosis with relation to RF-EMF exposure are presented.

METHODOLOGY

Published information was collected on myelin and myelin damage, related diseases such as multiple sclerosis, relevant cellular changes, and the functional impairment electrohypersensitivity, by using conventional scientific literature databases, such as biomedical literature from PubMed, Medline, life science journals, EMF-Portal, and online books, available on the Internet.

MYELIN AND ITS DEVELOPMENT

Myelin is a fatty membrane that provides insulation that enables rapid propagation of electrical impulses along nerves. Myelin is produced by two types of glial cell, oligodendrocytes and Schwann cells, and is primarily composed of water, lipids, and protein. Within the myelin, there are interlinked hydrocarbon chains of sphingomyelin, which provides a strengthening framework (Mandal, 2014). Sphingolipids also play important roles in signal transduction (Healy, 2008). Disorders in sphingomyelin result in lack of sphingomyelin phosphodiesterase (SMase). SMase is a hydrolase enzyme whose role is to degrade sphingolmyelin in phosphocholine and ceremide. This prevents buildup of sphingomyelin in the brain, bone marrow, and liver, which would otherwise result in impaired motor skills, muscle strength, vision and hearing problems, and ultimately death (Healy, 2008).

Myelin develops spirally around neuronal axons, creating a sheath that increases in effectiveness as it thickens. Oligodendrocyte cells are found only in the central nervous system (CNS), and each cell myelinates the axons of several neurons, while Schwann cells are responsible for myelinating the peripheral nervous system (PNS), there being one cell for each axon (Bear et al., 2007). There are small gaps in the myelin sheath at the axon hillock and at locations called the nodes of Ranvier. At these points, ions cross the axon to create action potential, thus boosting the signal along the axon.

If myelin is damaged, the impulses traveling along the nerves slow down. Apart from crush injuries, initiation and mechanism for myelin damage are not understood but are considered to be related to environmental or genetic factors. If myelin is not repaired, this results in a variety of symptoms and diseases. The most common of these is the autoimmune condition multiple sclerosis, which affects the CNS (Table 1). Conditions that affect the PNS include Guillain-Barré syndrome and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). CIDP is thought to be an autoimmune condition and is generally characterized by fatigue and increasing weakness, tingling, and pain in the limbs, beginning at the toes and fingers (National Institute of Neurological

TABLE 1. Symptoms Reported by People After Exposure (or Presumed Exposure) to RF-EMFs With Symptoms of Demyelination

	Symptoms of electrohypersensitivity	Symptoms of demyelination
Vision	Difficulty in seeing, smarting, pain	Blurred vision Progressive vision loss/blurring (children), pain, light flashes (children)
Motor	Trunk/limb/joints aches, pain Numbness Weakness	Trunk/limb weakness Numbness Weakness and fatigue Balance problems
Sensory	Tickling, prickling, burning sensations (ie numbness, paraesthesia)	Numbness, paresthesia (i.e., tickling, prickling, burning sensations)
Cerebellar	Tremor Faintness Dizziness Sleep problems Headaches Abnormally tired/sleep problems	Tremor Ataxia (reduced muscle control, incoordination) Seizures (children) Balance problems (children) Lethargy (children)
Cognitive/neuropsychiatric/ emotional	Short and long term memory impairment Lack of concentration Difficulty learning new things Irritability Anxiety Stress (feeling of lack of control) Mood changes (including anger) Depression	Memory impairment Concentration impairment Irritability Anxiety Confusion (children)

Note. Sources: ESUK (2014); Mar (2014); National Multiple Sclerosis Society (2014).

Disorders and Stroke, 2014). It is most common in young men.

Humans are born with scant electrical insulation of their nervous system. During development, a sheath of fatty myelin begins developing, first around axons in the CNS, then also sheathing peripheral and increasingly thinner axons (Wheeler, 2009). Once developed, it acts as electrical insulation and prevents the electrical signaling along the neuron from leaking out through the walls of the neuron. Its purpose is to enable efficient, speedy conduction of electrical nerve impulses. The major development of CNS sheathing occurs during the fourth and fifth months of gestation, continuing from the wk 25 of gestation until the age of 2 yr (Rathus, 2010), but age-related changes to axon thickness and white matter density visible in magnetic resonance imaging (MRI) scans indicate that it continues throughout childhood and adolescence (Paus et al., 1999). Myelination begins in the brainstem and cerebellar regions, progressing through to the frontal lobes during adolescence (Yakovlev and Lecours, 1967), and thereafter repeating in cycles. Wheeler (2009) suggested that myelination development, repair, and replacement continue throughout the CNS and PNS until late middle age, coating smaller and smaller diameter axons in increasingly thinner layers. The myelination of the splenium (located at the posterior end of the corpus callosum) is central to the efficiency of interhemispheric synchronization; this occurs over a protracted period (Knyazeva, 2013). Bartzokis (2011) proposed a theory that optimal brain function relies on finely tuned action potential synchronization, which myelin enables, but that in the presence of oxidative and environmental abnormalities and stressors, epigenetic changes result, leading to developmental and degenerative diseases. Being fatty, myelin does not contain free ions. Keshvari et al. (2006) postulated that this indicates that as the myelin sheath develops there is also a reduction in electrical conductivity of brain tissue. The reverse side of this coin is

that there is a higher overall electrical conductivity in the fetus, infant, and young child brain, as well as in those whose myelin has begun degenerating. Myelin deposition is delayed in malnourished children (Rodier, 2004), thereby possibly leaving some of lower socioeconomic status more vulnerable.

Excessive production of synaptic connections during fetal development is followed by heavy perinatal pruning; a second round, in the prefrontal cortex, occurs later with a marked rise in synapses at the onset of puberty (Huttenlocher, 1979), followed by pruning and reorganization during adolescence (Blakemore and Choudhury, 2006). This process is not complete until early adulthood. Rodier (2004) suggested that because prenatal CNS and myelination developmental processes are highly vulnerable to damage by environmental agents, it is reasonable to expect that brain development during childhood and adolescence also faces particular risks.

RF-EMF RESEARCH

The most relevant studies available were undertaken in the 1970s. In considering chronic effects, Switzer and Mitchell (1977) exposed 6-wk-old rats (5 h/d, 5 d/wk for 22 wk) to continuous-wave 2450-MHz RF-EMR (SAR 2.3 W/kg). There was a gap of 6 wk after exposure before analysis. Analysis using an electron microscope indicated a significant elevation in the number of myelin figures protruding into the cortical dendrites of the radiated, compared to control, subjects. No other striking structural changes were apparent. Baranski (1972) exposed guinea pigs and rabbits. Different guinea pig groups had exposures of 3.5 mW/cm^2 or 25 mW/cm^2, each being either continuous or pulse modulated. Exposure was at 3000 MHz, for 3 h daily for 3 mo, or the same frequency for a single 3-h session. The rabbits experienced 3 mo of chronic exposure at 5 mW/cm^2. Resulting damage was the same with both types of irradiation, but lesions were more marked and extensive from pulsed transmissions. Baranski (1972) found spherical metachromatic bodies in the myelin with large spheres in nervous tracts and glial cells, and smaller ones near the third ventricle and reticular formation structures, particularly around blood vessels within the myelin. These spheres were attributed to metabolic disturbances in the myelin sheath and particularly in the oligodendrocytes. Demyelination was indicated by a Marchi's reaction test. Some hyperchromatic cell bodies in the white matter had spirally twisted neurites typical of "chronic Nissl's disease." It should be noted that exposure at 25 mW/cm^2 produced thermal damage, and that 3.5 mW/cm^2 exceeds the public exposure reference levels, although falling within occupational exposures. Further, 2.3 W/kg is higher than permitted under International Commission on Non-Ionizing Radiation Protection (ICNIRP) or Institute of Electrical and Electronics Engineers (IEEE) standards. However, no temperature increases were evident at 3.5 mW/cm^2 or 2.3 W/kg. The greater impact of pulse-modulated exposures reported by Baranski (1972) is of great importance, since all present-day digital microwave radiation types are pulsed. This occurrence is explained by the ion forced-vibration theory (Panagopoulos et al., 2002), supported theoretically more recently by Halgamuge and Abeyranthe (2011).

OTHER RESEARCH RELEVANT TO MYELIN LOSS AND RELATED SYMPTOMS

A national Danish cohort study compared the country's MS register against private mobile phone subscription holders and nonholders prior to 1996 (Poulson et al., 2012). Despite the most basic estimate of exposure (phone ownership or not), there was one subgroup of account holders with significant elevated incidence, namely, women with >10 yr of mobile phone subscription (RR 2.08, 95%CI: 1.08-4.01; $n = 9$). A few MS onset symptoms were also significantly related, although different for men and women. Women had an increased incidence of fatigue (RR 3.02, CI: 3.02–6.28),

while men experienced an elevated frequency of optic neuritis (RR 1.38 CI: 1.03–1.86). Diplopia (blurred vision) was not significant in either group separately, but together the incidence risk rate was 1.38 (CI: 1.02–1.86). Finally, there was an elevated risk of death in MS patients with subscriptions 7–9 yr after MS diagnosis compared to those without subscriptions (RR, 2.44; 95% CI: 1.20–4.98; $n = 8$); however, it should be noted that the number in this category was small. The study excluded corporate subscriptions, which are likely to have been the highest users at that time. Since these are also likely to have been predominantly accounts for use by men, this may explain the significant MS results being in a subgroup of women.

Schüz et al. (2007) investigated a possible link between cellular telephone use and risks for various CNS diseases. In their large nationwide cohort study of 420,095 persons in Denmark, no marked associations for amyotrophic lateral sclerosis, multiple sclerosis, or epilepsy (in women) were observed, but there was an excess of migraine and vertigo connected to the mobile phone use. Elsewhere, rats were exposed to both 1.5 W/kg and 6 W/kg (GSM [global system for mobile communications] pulsed modulation) (Anane et al., 2003). There was a significant rise in amplitude of induced experimental allergic encephalomyelitis crisis between sham and real exposure at 1.5 W/kg (which is a permitted exposure in the ICNIRP and IEEE guidelines) but not at 6 W/kg, despite no marked difference in onset, duration, or termination. This condition is an inflammatory demyelinating disease of the CNS. The abstract does not mention this increase.

A small study published in 2007 found no gross effects on measured human cortical parameters in either healthy participants ($n = 10$) or MS participants ($n = 2$) (Inomata-Terada et al. 2007). Subjects were exposed to an 800-MHz pulsed signal for 30 min at the maximum permitted power output, using an adapted hand-held phone. For those with MS, exposure was before and after a hot bath, which generally brought on MS-related weakness. These data were unable to be analyzed statistically and were assessed individually by observation.

Symptoms of myelin loss include numbness and paraesthesia. An explanation is that alterations of myelin as well as Schwann cells of the sensory nerves may lead to functional alterations, slowing down of nerve signal conductance, and changes of nerve terminal sensitivity, which would lead to sensations of numbness and paresthesia, with the latter forming conscious thoughts via the spinal cord, thalamus, and primary as well as associative sensory brain cortex.

The skin is the organ most exposed to RF-EMF. Effects of EMF exposure on the skin were published in the 1960s. In experiments with rats, low-intensity exposure (≤ 1 mW/cm^2) reduced nucleoprotein content of various cells and tissues. Thereafter, marked morphological changes were observed in the receptor and interoceptor apparatuses for skin after exposures of 1 mW/cm^2, with slight changes noted elsewhere, including intestinal wall, the wall of the bladder, and aorta (Gordon et al., 1963). This study also found slight morphological changes in the axon-soma and axon-dendrite interneuron connections of the cerebral cortex. These effects were reversible, disappearing after 3 to 4 wk. Some reactions were only seen with frequencies below 3GHz, suggesting that the degree of functional and morphological changes depended on the wavelength.

There are also studies indicating involvement of cells or proteins related to production of myelin. Peinnequin et al. (2000) found that 2.45-GHz nonthermal exposure of Jurkat T cells over 48 h initiated Fas-induced apoptosis. When considered with other results, there was the potential that exposure affected either membrane proteins through the Fas receptor or SMase activation, or the Fas pathway between receptor and caspase-3 activation. In a study exposing human bone-marrow mesenchymal stem cells to a 1-mT 50-Hz field for 12 d, oligodendrocyte protein O4 was induced (Cho et al., 2012). Data indicated that in toto ELF might induce neural differentiation in these

cells. Hardell et al. (2010) determined the risk of oligodendroglioma and mobile or cordless phone exposure in deceased cases from certain areas of Sweden who were diagnosed with this tumor between 1997 and 2003. Results revealed a high odds ratio (OR) for those with >10 yr of phone use (OR = 10, 95% confidence interval [CI] = 1.1–89), but this was based on only 2 cases in this category, out of 9 who died from this tumor.

The presence of intraepidermal nerve fibers was investigated in normal human skin from healthy volunteers using the new marker PGP 9.5 (Wang et al., 1990). The intraepidermal nerve fibers are found as close as 20–40 μm from the surface, which makes it highly possible that weak EMF may affect them. In facial skin samples of electrohypersensitive persons, the most common finding was a marked rise of mast cells (Johansson and Liu, 1995). From these studies, it is clear that the number of mast cells in the upper dermis is increased in the EHS group. A different pattern of mast cell distribution also occurred in the EHS group, namely, the normally empty zone between the dermo-epidermal junction and mid- to-upper dermis disappeared in the EHS group and, instead, this zone had a high density of mast-cell infiltration. These cells also seemed to have a tendency to migrate toward the epidermis (= epidermiotrophism), and many of them emptied their granular content (= degranulation) in the dermal papillary layer. Further, more degranulated mast cells could be seen in the dermal reticular layer in the EHS group, especially in those cases that had the mast-cell epidermiotrophism phenomenon just described. Finally, in the EHS group, the cytoplasmic granules were more densely distributed and more strongly stained than control, and generally, the size of the infiltrating mast cells was noted to be larger in the EHS group. It is noteworthy that increases of a similar nature were demonstrated at a later experimental study employing normal healthy volunteers in front of cathode ray tube (CRT) monitors, including ordinary household television sets (Johansson et al., 2001).

A COMPARISON OF SYMPTOMS OF ELECTROHYPERSENSITIVITY AND DEMYELINATION

If myelin sheathing were compromised by repeated or chronic exposures to RF-EMF, one might expect to see an elevation in typical symptoms of demyelination. Specific symptoms depend upon the particular disease, which are diverse and include blurred vision, trunk/limb weakness, numbness, paresthesia, tremor or reduced coordination, memory impairment, reduced concentration or processing speed, depression, irritability, and anxiety (National Multiple Sclerosis Society, 2014). MS is unusual in children; however, symptoms they encounter include confusion, alteration of consciousness, lethargy, and visual symptoms including pain and flashes of light (Mar, 2014).

These symptoms have also been described as symptoms of EHS, although generally in lay language such as tickling/prickling sensations as opposed to paresthesia (Table 1).

Onset of any of these symptoms in these circumstances has come to be called electrohypersensitivity, although any one person may have a different set of symptoms from another. It should be noted that in a systematic review of both short-term exposure and epidemiological studies to investigate such claims, the overall evidence to support them was thin (17 out of 117 potentially eligible papers were included after checking the qualifying criteria set by the research group) (Röösli et al., 2010). Johansson (2006, pp. 245–246) recorded early symptoms of electrohypersensitivity as "itch, smarting, pain, heat sensation, redness, papules, pustules . . . [and] frequently [symptoms related to] internal organ systems, such as the heart and the central nervous system, are also encountered." According to Sweden's National Board of Health and Welfare, the most commonly reported symptoms of electrohypersensitivity are fatigue, difficulty in concentrating, dizziness, nausea, palpitations and digestive disturbances (Socialstyrelsen (The National Board of Health and Welfare) 2014).

The British organization ElectroSensitivity United Kingdom (ESUK) describes symptoms

such as those itemized in the left column of Table 1 (ESUK, 2014). There have been reports of cardiovascular problems such as tachycardia and arrhythmia, although these are relatively rare. Havas (2013) demonstrated these symptoms in double-blind, sham-controlled circumstances.

DISCUSSION

Despite early indications of damage to myelin sheathing in animals exposed to RF-EMF in the 1970s, there has been remarkably little research follow-up. There is still a lack of basic experimental evidence for a clear association between myelin damage and electrohypersensitivity, but given the preceding hypothesis it would be of great interest to investigate this in more detail using classical immunohistochemical markers for healthy and degenerated myelin, respectively, and for Schwann cells in general. Since myelin is the main electrical insulation that ensures efficient electrical functioning of the CNS, its integrity is vital to this, and healthy development of the neuronal system may also be. Therefore, it is important to know whether or not it is damaged by exogenous RF-EMF exposures.

What evidence is there that it may be? There do not appear to be national registers for MS, but the UK Multiple Sclerosis Trust reports that prevalence in women is increasing (Multiple Sclerosis Trust 2014). Race and latitude have been identified as influential in risk, but that incidence may be modified by the environment (Rosati 2001). When a child uses a wireless phone against the head (held at the usual angle), the most exposed area in that child's brain is the cerebellum (Christ et al. 2010); this is one of the first areas myelinated. As the head size nears adulthood, and depending upon head geometry, the most exposed area becomes the temporal lobes. This suggests that during adolescence the temporal lobes may be more susceptible to RF-EMF interference, not only because this region is not yet fully myelinated at that age, but because of enhanced vulnerability during active synaptic rearrangement and pruning in progress at that age.

Demyelination and electrohypersensitivity have many symptoms in common. This latter condition is frequently regarded as psychosomatic, with the symptoms being claimed to be subjective, nonspecific, and hard to test objectively. However, these symptoms clearly point to a common, highly specific, biological and behavioral avoidance reaction and most can easily be objectively studied and quantified. For instance, the subjective sensations of tingling in the skin, itching, and heat may all be explained by changes in biochemical markers, especially histamine of the mast cells, observed by Johansson (2006).

A review of provocation studies of electrohypersensitives investigations generally did not show a significant response compared with control groups (van Rongen et al., 2009); however, it was acknowledged that such studies are often disadvantaged by short exposure durations.

The symptoms of the two conditions, demyelination and electrohypersensitivity, are not entirely matched. Reduced muscle control (ataxia) is an important symptom of demyelination, as are seizures and balance problems in children, but infrequently reported as a symptom of RF-EMF exposure, although the more minor cerebellar conditions of tremors and dizziness are. On the other hand, there are a few symptoms such as headache, tinnitus, heart arrhythmia, and skin problems that are commonly reported from RF-EMF exposure but are not symptoms of demyelination.

An increased heart rate, altered heart-rate variation, and changes in the sympathetic and parasympathetic control of the autonomic nervous system have been objectively tested and demonstrated as associated with RF-EMR exposure in more than one study (Havas and Marrongelle 2013). Headaches have been associated with exposure in several epidemiological studies. In a review by Augner et al. (2012), there were in total 737 participants in 8 studies who evaluated headaches with relation to RF-EMF exposure and demonstrated an overall marginal association of headaches

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CASE REPORT

Exacerbation of demyelinating syndrome after exposure to wireless modem with public hotspot

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ABSTRACT

In August 2003, 48-year-old JS of Colorado, USA, a fitness therapist and sports nutritionist, contracted neuroinvasive West Nile virus which left her with disabilities due to spinal axonal damage.

In August 2014, she suddenly developed symptoms very much like her acute West Nile infection 11 years ago, including focal seizures, ataxia, vertigo and headaches. Her blood count looked normal so there was no obvious infection. What struck her as odd was that when she left her apartment for any length of time, the symptoms stopped. She found out that a new type of wireless modem, enabled for both personal use and functioning as a public hotspot designed to reach up to 100 m, had been installed in the flat under hers.

Her neighbor replaced the modem with a router without the hotspot feature. After that, the seizures stopped immediately, and the other symptoms faded gradually, after which she was fine and again could sleep well. Later, when another activated hotspot was installed in an adjacent flat, JS once again noticed symptoms.

A possible association between electrohypersensitivity, myelin integrity and exposure to low-intensity radiofrequency electromagnetic fields (RF-EMF) typical in the modern world has recently been proposed. Since the West Nile virus attacks both the nerve cells and the glial ones, one explanation to the above observed case effects is that the initial virus attack and the wireless modem's RF-EMF affect the nervous system through the very same, or similar, avenues, and maybe both via the oligodendrocytes.

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Beacon signal; electrohypersensitivity; hotspot; myelin; neurodegenerative disease; radiofrequency exposure; strobe effect; WiFi

Background

In August 2003, 48-year-old JS of Colorado, USA, a fitness therapist and sports nutritionist contracted neuroinvasive West Nile virus which left her with disabilities due to axonal damage in the cervical and thoracic spine. Laboratory tests at the time confirmed anti-myelin antibodies and anti-ganglioside antibodies. The subsequent damage led to focal seizures, headaches, ataxia, paresthesia and vision problems which gradually improved over the subsequent 2 years. She worked hard to overcome many of the effects of her illness, but still had to be very careful about attracting any form of inflammation and is still officially disabled. She could no longer live in her home because she had to have wheelchair access. It took a couple of moves to find an ideal living situation, but she was eventually able to secure a third-floor unit in a handicapped accessible senior complex (55+) where she lived happily since then.

The only regular medications she takes are replacement thyroxine, steady since 1982. She never takes non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin.

In August 2014, she suddenly developed symptoms very much like her acute West Nile infection 11 years ago, including focal seizures, ataxia, vertigo and headaches. Her blood count looked normal so there was no obvious infection, but she was losing sensation in her face, neck and torso. What struck her as odd was that when she left her apartment for any length of time, the symptoms stopped. It took some investigating, but she found out that a new type of wireless modem had been installed in the unit under hers. She herself used a cell phone, a wireless router and a computer and had no problems with those products. However, she found out that this new wireless modem was enabled for both personal use and functioned as a public hotspot designed to reach up to 100 m, but was just feet below her floor.

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Because of the severity of the reaction, she asked her neighbor if he would be willing to turn off his modem at night so that she could sleep without seizures preventing this. He was very concerned and turned off the modem completely and replaced it with a router that was compatible with the service in question but that did not have the hotspot feature. After that, the seizures stopped immediately, and the other symptoms faded gradually, after which she was fine.

Nine weeks later, on 7 November, the symptoms started again. It took some weeks to locate the source. Finally, she found out that another of these modems had been installed, this time across the hall from her unit. On 10 December, the owner disabled the hotspot component. JS found she was able to sleep in her bedroom for the first time in weeks with none of the symptoms.

From before the episodes occurred, JS has kept her mobile phone WiFi disabled while at home. The day after she began having symptoms in August, she had temporarily enabled the WiFi feature while out shopping and when she came home that day, a pop-up appeared informing her she was in a free Xfinity WiFi zone. She checked the connections and saw the new router name and signal strength on the list. Since a new tenant had just moved in below her, she asked him if he had had a new modem installed, which he confirmed. Because her own wireless modem had not been a problem, she did a search online and found out about the new marketing plan that Comcast was implementing using customers' personal modems to provide 1 h of free hotspot use along with advertisements encouraging users to sign up for their own account.

There are still strong signals in her unit from four modems, but none of them are hotspots, and do not cause her problems. There are also signals of the sort with hotspots from the far end of the building that have not caused JS any problems at the time of writing. Their pop-ups do not appear on her phone unless she walks along the corridor toward them.

There have been suggestions that the functional impairment electrohypersensitivity is psychosomatic (Landgrebe et al., 2008). This may be the case in some instances; however JS has never been diagnosed with or treated for depression, anxiety or related disorders, and the symptoms appeared well before she identified a source that, repeatedly, appeared correlated.

Clinical

On 8 September 2014, JS revealed changes in her memory B cells (IgD+/CD27+ low; IgD-/CD27+ low; IgD +/CD27– high), and in 19 November 2014, she was tested high for IL-4 (in a TH1/TH2 Panel Test). IL-4 is an inflammatory cytokine consistent with upregulated mast cell response. From such single tests it is, of course, very difficult to draw any conclusions; the blood test may merely be showing random alterations due to having had the West Nile virus poliomyelitis. But, it could also be due to the influence of electromagnetic field exposures (cf. Johansson (Johansson, 2009), including them affecting the mast cells.

Reported fluctuations in response

JS noticed differences in symptoms according to the time of day/night and the distance from the router with the public hotspot, and whether or not the hotspot component was activated or disabled. Distance from, and activation of, the router was generally only ascertained after experiencing symptoms. This was done using a mobile phone application that graphs wireless connections when JS experienced symptoms.

When there was an activated hotspot in an adjacent unit, JS noticed symptoms. This occurred prior to knowing one was there and recurred when a new one was installed nearby without her knowledge.

On getting out of bed in the morning, she often experienced temporary vertigo, tinnitus and allergy symptoms like those of severe hayfever. Other common symptoms were headache, difficulty concentrating, poor fine motor control, impaired short-term memory and pain in the facial bones, especially the malar bone (cheeks) and mandible (jaw) including the roots of the teeth. There were no sinus infections or colds during the weeks the hotspots were active.

If she left the house for a while, mental symptoms diminished. Other daytime symptoms included numbness, tingling and difficulty breathing and swallowing and were also more pronounced after exertion. Other physical symptoms of ringing in ears and dizziness also diminished when leaving the house temporarily, but the November/December exposure was considerably longer and the numbness and other typical demyelination symptoms persisted for a while when out of the house.

In the evening, her appetite was much increased and she craved sweet food, which was not usual for her. She became sleepy at the usual time, settling down between 10.30 pm and 11 pm and could fall asleep, all as normal.

However, within 1–2 h, she routinely woke suddenly having had very vivid, disturbing dreams and with a pounding heartbeat. This was usually followed by a seizure, sometimes focal, where one part of her body (primarily right arm) would be shaking. Other times, her whole body was shaking. After a seizure, she slept

fitfully, unless she moved to sleep on the couch in another room. There, JS found she could fall asleep quite quickly and sleep through the rest of the night.

This type of seizure was documented as occurring twice during auditory evoked potential tests about 10 years ago. JS was told that she was having a seizure, but that it was related to the gray matter, not white matter part of the brain and therefore was not well defined on the electroencephalogram. Those seizures ceased within 2 years after contracting West Nile virus. This may indicate that the seizures were not epileptic, but due to myelin loss (Yarnykh et al., 2015).

After the recurrence of symptoms recently, JS discovered which neighbor had a WiFi system with public hotspot. The unit was diagonally across the hall which made the area with the modem just 20–30 feet from her bedroom, but about 50–60 feet from her living room (plus an additional wall), both of which would weaken the signal somewhat.

There was some sign of adaptation for some symptoms. The first time symptoms appeared in August 2014 the hotspot was only on for about 3 days. JS had very acute symptoms, and as soon as it was disabled they went away. The most recent exposure was over 4 weeks. During that time, she had the same acute symptoms and elevated morning fasting blood sugar levels (up 25% from usual to 100 mg/dL), but the neurological symptoms did seem to reduce with time. During the 4-week exposure, there was a fight or flight reaction for the first 2–3 weeks, which then turned into fatigue and apathy with little accomplished during the day. The day after the hotspot was disabled JS could focus on an activity for 4 h and felt much calmer. Her morning fasting blood sugar was back to normal 2 weeks later.

JS notices no effects from the private WiFi component once the hotspot component is disabled.

Relevant wireless protocols and operating frequencies

The symptoms outlined above have reportedly been experienced in relation to the public hotspot component of Comcast's Xfinity Gateway WiFi service, which is supported by Technicolor.

Depending upon the model, it can operate on either IEEE 802.11a/b/g protocols (Comcast, 2012) simultaneously, or IEEE 802.11b/g/n protocols. These protocols specify characteristics of the beacon signal which is transmitted typically over 1 ms of each 100 ms leading to a 10.24 Hz pulse with 1% of the time taken by the beacon; other pulse durations are sometimes used. The beacon signal continues as long as the router is turned on. When in use, the resulting duty signal increases the percentage of time the router is transmitting. All transmissions are at full power. The beacon signal contains all necessary information about the network to enable those within range to use the service. 802.11b and g are 2.4 GHz protocols, while 802.11a operates in a 5 GHz bandwidth. The most recent protocol, 802.11n, operates at either 2.4 GHz or in the 5 GHz bandwidth and has a greater range than the other three. Meter testing indicated the public hotspots near JS's apartment were functioning on 2.4 GHz. Reportedly, the Gateway contains two antennas, one of which is secured for the use of the paying customer and the other is available as a public hotspot (Hayes, 2014). The hotspot antenna almost certainly has a considerably higher transmit power as this would be needed to increase the effective transmit range for users in the area. WiFi signal range depends on several protocol factors including transmit power and transfer rate. Intensity falls away quickly with distance. Walls and vegetation reflect and absorb some of the signal, but do not block it. The 802.11b and 802.11g protocols fitted with standard antennae have a range of approximately 250 feet (76 m) (National Instruments, 2013), while that of 803.11n can be double of that (Belanger, 2007).

Measurements of the electric field and the power density were taken in the hallway, but are not presented as we were unable to determine the distance to the routers. JS declined a request to ask the residents as they are elderly and she did not want to worry them.

Signal strength (dBm) does not correlate well with her experienced symptoms. For instance, an Xfinity hotspot signal strength as low as −58 dBm,[1] equal to 0.002 μW, triggers the reported responses in JS, while other signal sources such as a mobile phone by the head and other WiFi signals prompt no symptoms, even with much higher exposures.

Discussion

A recent paper (Redmayne and Johansson, 2014) has pointed to a possible association between electrohypersensitivity, myelin integrity and exposure to low-intensity RF-EMF typical in the modern world. Overall, evidence from in vivo and in vitro and epidemiological studies suggests an association between RF-EMF exposure and either myelin deterioration which weakens neuronal transmission resulting in loss of muscle function, or a direct impact on neuronal conduction, which may result in the neuron hyperactivity, paresthesias and severe pain which are sometimes characteristic of electrohypersensitivity.

Since the West Nile virus attacks both the nerve cells and the glial ones, one explanation to the above observed case effects is that the initial virus attack and the wireless modem's RF-EMF affect the nervous

system through the very same, or similar, avenues, and maybe both via the oligodendrocytes.

The trigger of effect in this case is hard to identify as full details of the transmit protocol are not available and the provider has not responded to queries on hotspot specifications.

JS does not have EHS responses to signals other than this hotspot one, even though this RF-EMF exposure intensity from several meters away will be considerably lower than that from using her own mobile phone or computer. Although it appears the strength of the exposure is one determining factor, characteristics of the signal that differ from those from her own regularly used equipment are likely to be involved. This could be the beacon interval, if this is different than those generally encountered (e.g. if the hotspot had an interval of 200 ms it would result in a 5 Hz pulse). However, an audio recording of the beacon signal indicates this does not appear to be the case.

A second factor that may be a trigger is the pulse width of the beacon signal (on time). If this is longer than the standard 1 ms, the body may "notice" and respond to the extended duration of each 10.24 Hz pulse more readily. As an illustration, it is easier to see a line of dashes that take up 3% of the line than a row of dots that take up 1% of the line. Another possible explanation is an additional pattern or stroboscopic effect, or double intensity set up by the simultaneous transmission of the private and public hotspots.

A high transmit power from the hotspot would have little effect on the average power of the beacon signal since it only occupies a small proportion of the transmission. But the beacon along with another component, such as a 10.24 Hz frequency, could conceivably stimulate or trigger certain biophysiological responses, such as seizures in some people.

This explanation fits the scenario as transmit power decreases rapidly with distance and JS finds the symptoms only appear within a certain radius of the hotspot. If the pulse of the beacon signal component is the trigger, we put forward a hypothesis that the responses may be similar to those experienced by some people in response to strobe lighting, to which responses are highly individual and occur in 1 in approximately 4000 people (Harding, 1994).

In this case, a distance of at least 30 m from an enabled Xfinity hotspot is the only reliable identified variable needed for no symptoms to appear.

This case raises some concern for those in the population with currently well-managed demyelinating diseases such as multiple sclerosis. Technologies based on various artificial electromagnetic fields, such as microwaves, are increasing incrementally and public health infrastructure that could ameliorate harm remains inadequate. It will be a fundamental task to investigate the scientific background to our case observations, but they strongly indicate that emissions from these new wireless modems could cause physical harm for those susceptible to that type of radiation.

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Declaration of interest

The study had no other involvement from these or other companies.

The authors have had no writing/editorial assistance in preparing the paper, although confirmation was sought from JS and her doctor regarding the accuracy of the details of the reporting and minor amendments made accordingly. Mary Redmayne is a member of the Stds. Australia technical committee TE-007.

Note

1. Cornet ED 78S meter, margin of error +/−3.5 dBm.

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Report of Partial findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats (Whole Body Exposure)

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Abstract

The US National Toxicology Program (NTP) has carried out extensive rodent toxicology and carcinogenesis studies of radiofrequency radiation (RFR) at frequencies and modulations used in the US telecommunications industry. This report presents partial findings from these studies. The occurrences of two tumor types in male Harlan Sprague Dawley rats exposed to RFR, malignant gliomas in the brain and schwannomas of the heart, were considered of particular interest, and are the subject of this report. The findings in this report were reviewed by expert peer reviewers selected by the NTP and National Institutes of Health (NIH). These reviews and responses to comments are included as appendices to this report, and revisions to the current document have incorporated and addressed these comments. Supplemental information in the form of 4 additional manuscripts has or will soon be submitted for publication. These manuscripts describe in detail the designs and performance of the RFR exposure system, the dosimetry of RFR exposures in rats and mice, the results to a series of pilot studies establishing the ability of the animals to thermoregulate during RFR exposures, and studies of DNA damage. Capstick M, Kuster N, Kühn S, Berdinas-Torres V, Wilson P, Ladbury J, Koepke G, McCormick D, Gauger J, Melnick R. A radio frequency radiation reverberation chamber exposure system for rodents Yijian G, Capstick M, McCormick D, Gauger J, Horn T, Wilson P, Melnick RL and Kuster N. Life time dosimetric assessment for mice and rats exposed to cell

phone radiation Wyde ME, Horn TL, Capstick M, Ladbury J, Koepke G, Wilson P, Stout MD, Kuster N, Melnick R, Bucher JR, and McCormick D. Pilot studies of the National Toxicology Program's cell phone radiofrequency radiation reverberation chamber exposure system Smith-Roe SL, Wyde ME, Stout MD, Winters J, Hobbs CA, Shepard KG, Green A, Kissling GE, Tice RR, Bucher JR, Witt KL. Evaluation of the genotoxicity of cell phone radiofrequency radiation in male and female rats and mice following subchronic exposure

Key House and Senate members unveiled a bipartisan agreement Friday on a Federal Communications Commission reauthorization that would provide the agency with more than $330 million annually in fiscal years 2019 and 2020.

The agreement also resolves issues that were slowing spectrum auctions for wireless technology.

House Energy and Commerce Chairman Greg Walden, R-Ore., and Senate Commerce, Science and Transportation Committee Chairman John Thune, R-S.D., as well as ranking members Sen. Bill Nelson, D-Fla., and Rep. Frank Pallone Jr., D-N.J., said the agreement would promote next-generation wireless technology.

The "bipartisan, bicameral product puts consumers first and solidifies the nation's critical telecommunications infrastructure, giving the U.S. a global edge" in the race to develop fifth-generation, or 5G, wireless networks "and in improving improving internet services across the country," they said in a joint statement.

The House is expected to vote on the bill next week under suspension of the rules, an expedited procedure that limits debate and amendments and requires a two-thirds majority for passage. The text of the measure is expected to move as an amended version of the committee-approved House FCC reauthorization bill, sponsored by Rep. Marsha Blackburn, R-Tenn.

The path to final Senate passage is unclear, although several senior Republicans said this week that such an agreement could move as a stand-alone measure or an add-on to other legislation.

According to a 108-page draft released Friday by the House Energy and Commerce Committee, the bill would provide $333 million to the FCC in fiscal 2019 and $339 million in fiscal 2020. The funding would be more than the $322 million in annual funding for fiscal 2019 and 2020 provided in the House version of the FCC reauthorization approved by the Energy and Commerce Committee by voice vote on Feb. 14.

According to a summary of the agreement, it would include a provision aimed at clearing the way for future spectrum auctions by making clear that funds from spectrum bids could be placed in the Treasury and not in a private bank or in the Federal Reserve.

FCC Chairman Ajit Pai praised the leaders of both panels in a tweet Friday morning for "forging an agreement that would allow" the agency to carry out spectrum auctions, including two planned auctions aimed at expediting development of 5G networks that he outlined in a speech to the Mobile World Congress in Spain on Feb. 26.

In the speech, Pai said he would need Congress to "pass legislation by May 13 addressing the handling of upfront payments" contained in the FCC reauthorization, in order to start one of the auctions in November, as planned.

The measure would establish a fund — without specifying the amount of funding — to help broadcasters cover costs related to a pending reshuffling of spectrum slots after an incentive auction last year to make way for wireless providers.

The agreement would include a fund to reimburse television broadcasters and low-power television operators for giving up channels to accommodate wireless providers. The measure also would allow aid for FM radio station operators to help cover the cost of moving radio equipment related to the spectrum reshuffling.

The funds were a top priority for the National Association of Broadcasters, which praised the agreement in a written statement as as a "significant step toward fully reimbursing broadcaster 'repack' to help cover relocation costs."

A separate Pallone proposal would authorize $1 billion to compensate broadcasters for repack-related costs, but lawmakers have not reached consensus on the amount of funding for such expenses.

Thune won a key concession in the accord with the inclusion of language similar to his bipartisan Senate-passed proposal to identify for auction 255 megahertz of spectrum for mobile networks and wireless broadband.

Thursday, February 1, 2018

Effects of Exposure to Electromagnetic Fields: 833 Studies

Government and industry-linked scientists often claim that the research on the effects of exposure to electromagnetic fields (EMF) is inconsistent, and that more research is needed before precautionary warnings are issued or regulatory guidelines are strengthened.

Although most of the research on cell phones has focused on radio frequency radiation (RFR), these wireless devices also produce extremely low frequency electromagnetic fields (ELF EMF). The International Agency for Research on Cancer of the World Health Organization classified ELF EMF "possibly carcinogenic to humans" (Group 2B) a decade earlier than RFR.

Dr. Henry Lai, Professor Emeritus at the University of Washington and Co-Editor-in-Chief of the journal ***Electromagnetic Biology and Medicine***, has compiled summaries of several areas of the research on the biologic and health effects of exposure to RFR and ELF EMF. His sets of abstracts which cover the period from 1990 to 2017 constitute a comprehensive collection of this research.

Dr. Lai finds that the preponderance of the research has found that exposure to RFR or ELF EMF produces oxidative stress or free radicals, and damages DNA. Moreover the preponderance of RFR studies that examined neurological outcomes has found significant effects.

The evidence for DNA damage has been found more consistently in animal and human (*in vivo*) studies than in studies of cell samples (*in vitro*).

The abstracts can be downloaded from the BioInitiative web site by clicking on the links below.

Top Line Results

Radiofrequency radiation:

- 90% (n=180) of 200 oxidative stress (or free radical) studies report significant effects.
- 64% (n=49) of 76 DNA comet assay studies report significant effects.
    - 54% (n=25) of 46 *in vitro* studies report significant effects.
    - 80% (n=24) of 30 *in vivo* studies report significant effects.
- 72% (n=235) of 325 neurological studies report significant effects.

Extremely low frequency electromagnetic fields:

- 87% (n=162) of 186 oxidative stress (or free radical) studies report significant effects.
- 74% (n=34) of 46 DNA comet assay studies report significant effects.
    - 68% (n=21) of 31 *in vitro* studies report significant effects.
    - 87% (n=13) of 15 *in vivo* studies report significant effects.