Microwave Electromagnetic Radiation and Autism

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Abstract

Child numbers with autism spectrum disorders (ASDs) and population exposure to microwave irradiation have risen in parallel. It has been suggested that fetal/neonatal microwave exposure might predispose to later ASD development. The hypothesis has been evaluated through consideration of three aspects. First, plausibility was addressed through review of potential mechanisms: the presence of magnetite in human brain, with pulse modulation of microwave signals in a frequency band critical for synaptic plasticity, suggests that microwave radiation could interfere with brain development and function. Second, typical levels of domestic microwave exposure were compared against recorded effects of gestational exposure of experimental animals. The highest recurrent exposures are from mobile/cordless phone handsets and domestic base-stations (up to 20 microW/cm^2) whereas continuous gestational exposure of rodents at 100 microW/cm^2 was not reported to produce adverse behavioral changes. Third, the timing of the first rise in ASD was compared against that of the spread of domestic microwave devices. In the USA and other western countries, ASD diagnoses began to rise sharply in the early 1980s. Microwave ovens first reached western households in the early 1980s, becoming commonplace by the mid-1980s; uptake plateaued from 1990 while ASD rates have continued to rise. Mobile and cordless telephones were rare until 1995, a decade later than the rise in ASD. The data overall do not yet provide support for the hypothesis, but the ongoing rise in microwave communications may warrant official surveillance of exposure levels.

Keywords: *Autism; Autism Spectrum Disorder (ASD); Electromagnetic; Environment; Microwave; Radiation*

Introduction

The prevalence of autism spectrum disorders (ASDs) has risen over the last two decades. At the same time, population exposure to microwave electromagnetic radiation has increased. It has been proposed that microwave exposure in the prenatal/postnatal period might predispose to such disorders (Kane, 2004).

ASDs are diagnosed early in childhood, with warning signs in the postnatal period. Although known genetic defects, such as Fragile X, predispose to ASD development, in the absence of any known genetic factor the disorders can be precipitated by maternal medication during pregnancy. Gestational exposure to alcohol, anticonvulsant medication, cocaine, thalidomide and tobacco are all risk factors for ASD development in the child (Lathe, 2008). Some ASD cases have been attributed to congenital infection with rubella or cytomegalovirus, while a small group of children injured by perinatal hypoxia developed severe infantile autism (DeLong & Heinz, 1997). These observations indicate that many ASD cases, if not the majority, can be attributed to adverse influences during gestation and/or the postnatal period.

The rise in ASD rates implicates an environmental factor. Once very rare, affecting less than 1-10 per 10,000 population, prevalence is now 116 children per 10,000 in London (Baird et al., 2006) while ASD rates in the USA approach 1% in younger age groups (Centers for Disease Control and Prevention, 2006). Although diagnostic substitution could account for some of the rise, a large survey failed to substantiate this contention (Newschaffer, Falb, & Gurney, 2005); autism prevalence rose 10-fold over a decade in Minnesota despite using identical diagnostic criteria (Barbaresi, Katusic, Colligan, Weaver, & Jacobsen, 2005). A 10% annual increase was recorded in Canada, with highest rates (107 per 10,000) in the younger children (Fombonne, Zakarian, Bennett, Meng, & McLean-Heywood, 2006). However, the specific environmental factor remains unknown, and prenatal/postnatal microwave radiation may be a contender (Kane, 2004). Furthermore, there has been a recent report that children (n=10) developing ASD were exposed in utero to higher levels of electromagnetic radiation than controls (n=5) (Klinghart, 2008); nevertheless the sample sizes were small and statistical significance was not addressed.

The objective of this survey is to evaluate the hypothesis with regards to three specific questions. First, is the hypothesis plausible? Potential biological mechanisms are considered whereby microwave radiation might have an adverse impact on brain development and function. Second, is the power density typically encountered at a level known to produce behavioral anomalies? This is addressed through consideration of likely exposure levels in the household and through review of studies on experimental animals that record the behavioral outcome of gestational exposure. Third, is the time-frame of the rise in ASD compatible with the rise in

microwave exposure? Evaluation is through review of historic uptake rates of relevant microwave devices including mobile telephony and domestic microwave heating appliances. Before turning to address these specific questions, the types of exposures encountered by the general population are briefly overviewed.

Electromagnetic Radiation: Sources of Exposure

All life-forms are exposed to electromagnetic fields, most prominently from the natural magnetism of the Earth. Some studies have pointed to adverse biological effects of high-intensity static magnetism but it is generally assumed that such fields, within the intensity range of natural magnetism, are unlikely to be of significant health impact.

Artificial oscillating electromagnetic fields are of greater concern. Historically, mains power afforded the first population exposure but the low power density and timing of the introduction (in the early 20th Century) is not consistent with a contributory role in the recent rise in ASD. High-voltage power transmission lines (above 100,000 V) may present a greater health risk (SAGE, 2007) but the majority of the population is not exposed. In contrast, there is now widespread population exposure to high frequency (MHz/GHz) radiation in industrialized countries. Major sources include mobile communication systems, commercial radio and television broadcasting, aviation and marine radars, satellite communications, microwave frequency heating devices, and domestic 'wi-fi' equipment including digital enhanced cordless telephony (DECT). Of these, microwave ovens and mobile communication devices are likely to provide the highest exposures for the general population.

Different units are employed to measure and compare exposures. These include V/m (electric field strength), A/m (magnetic field strength) and the heating effect of the radiation in W/kg. At a distance from the antennae the incident power per unit area affords the most appropriate unit of measure, commonly Watts per square meter (W/m^2) or mW/cm^2 (1 W/m^2 = 0.1 mW/cm^2) termed the irradiance or power density.

As a tangible reference point, full sunlight in the visible range (not microwave) at the Earth's surface equates to around 100 mW/cm^2, an intensity sufficient to produce heating in exposed tissue. Microwave radiation from natural sources is at least a million times lower. However, it remains an area of debate whether microwave exposure can produce biological effects at intensities below a level likely to produce any detectable thermal effects.

Microwave Ovens

Emissions from microwave ovens are generally limited by legislation: in the USA the Food and Drug Administration (FDA) specifies a maximum of 5 mW/cm^2 at a distance 5 cm from the oven surface with an estimated irradiance at 50 cm of 0.05 mW/cm^2 (FDA, 2007). In other countries the International Commission on Non-Ionizing Radiation Protection (ICNIRP) guidelines apply, limiting emissions to 1 mW/cm^2 (ICNIRP, 1998). The majority of domestic appliances operate at 2.45 GHz, though different frequencies have been used (notably 915 MHz in some industrial heaters). Signals from some appliances are modulated at mains power frequency (50-60 Hz) (Kamerman & Erkoçevic, 2008).

Mobile Telecommunications

Prior to 1992 the major networks were analog (0.8 GHz, frequency modulated), now largely discontinued. Other systems include North American Digital Cellular (NADC) technology (0.8 GHz, pulsed at 50 Hz) but currently over 80% of users worldwide use the GSM (Groupe Spécial Mobile) system. Most networks operate in the 0.85-0.9 and/or 1.8-1.9 GHz bands, pulse modulated at 217 Hz, though rarer 400 and 450 MHz frequency bands have been assigned in some countries, notably Scandinavia. Early (1981) emission limits ranged from 0.1-100 mW/cm^2 (around an approximate midpoint of 1 mW/cm^2) according to country (IPCS, 1981). Worldwide, diverse restrictions are in place, as compiled (International EMF Project, 2008), but guidelines laid down by the ICNIRP are increasingly adopted in many countries.

The basic limit for general public exposure is set to 1 mW/cm^2 (ICNIRP, 1998). This recommendation has been followed by the European Union (CEU, 1999). In the USA and Canada, the basic restriction level is also 1 mW/cm^2 in the GHz range; while in the UK exposures above 10 GHz are limited to 10 mW/cm^2 but limits for lower frequencies (10 MHz – 10 GHz) are defined in terms of specific absorption rate (SAR) in W/kg, complicating assessment. For the purpose of discussion, it is assumed that a basic limit of 1 mW/cm^2 is respected by mobile phone manufacturers and network operators in the majority of countries, though an uncertainty arises concerning the degree of compliance.

DECT and DFHSS

Almost all cordless telephones use the 900-MHz, 1.9-GHz, 2.4-GHz, or 5.8-GHz bands. In Europe, DECT operates at 1880-1900 MHz in Europe, and between 1920 and 1930 MHz in the USA. Like GST mobile telephones, DECT is modulated, but at 100 Hz rather than 217 Hz. A parallel USA system Digital Frequency Hopping Spread

Spectrum (DFHSS) operates at higher frequency (2450 MHz) but is also digitally pulsed at 100 Hz. Typically DECT and related systems are employed for 'walk around' domestic telephones with signals being relayed from a base-station inside the home. Mobile computer access ('wi-fi') operates using a similar system.

Recorded Exposures (Mobile Telephony)

Two types of exposure are encountered: emissions from base-station masts and local emissions from hand-held devices. In systematic assessment of irradiances from masts the National Radiation Protection Board (NRPB, UK) determined that power levels were in the broad range of 1-1000 microW/m^2 (<0.1 microW/cm^2) while the very highest level recorded at all sites was 0.83 microW/cm^2 on a playing field 60 m from a school building with a mast mounted on its roof (Mann, Cooper, Allen, Blackwell, & Lowe, 2000). This irradiance is 1000-fold below ICNIRP limits. The low figure is because antennae emit narrow beams in the vertical plane: field intensity directly below an antenna is lower than at a moderate distance (100-200 m). Average intensity (all sources considered) was 0.011 microW/cm^2 and highest (top 5% of all sites) 0.1 microW/cm^2.

Survey of emissions in different geographic areas of Sweden recorded a maximum irradiance overall of 0.3 microW/cm^2 outdoors in a town area, while at 100 m from a GSM base station only 0.16 microW/cm^2 was recorded (Hamnerius & Uddmar, 2000). The mean value of 26 sites was 0.05 microW/cm^2, in good correspondence with the NRPB study.

Higher levels have been recorded in close proximity to microcell antennae. A more recent NRPB survey reported intensities close (<30 m) to the antennae in the approximate range 0.2-20 mW/cm^2. The very highest exposure (20 mW/cm^2) was recorded a few meters from the antenna (Cooper, Mann, Khalid, & Blackwell, 2006) but field strengths declined rapidly to below 10 microW/cm^2 at 100 m. Levels of exposure of the general public were deemed negligible.

Exposure is substantially greater for hand-held mobile devices. To maximize communication distances such devices are presumed to operate, during the 'active use' mode (rather than during 'standby') at close to the ICNIRP limit of 1 mW/cm^2, pointing to irradiances of between 0.1 and 1 mW/cm^2 in the immediate vicinity of the device (1 cm), with a maximum irradiance of 10 microW/cm^2 at 10 cm or more. Despite this, some anecdotal accounts point to peak emissions of 10 mW/cm^2; this level of exposure would be more worrying but has not been confirmed.

Recorded Exposures (DECT/DFHSS)

Power densities can be high in the immediate vicinity of the emitting base-station. Based on a single report, irradiances up to 28 microW/cm^2 were recorded at 50 cm, but at a distance, for instance in the next room, power levels fall. In bedrooms adjacent to an office containing a DECT/DFHSS base-station the mean irradiance was 0.65 microW/cm^2 (Haumann & Sierck, 2002). However, unlike microwaves and mobile phones, exposure continues even when the device is not in active use, increasing total exposure.

Other Sources

In comparison, all other sources of EMR (including radio, television, radar, satellite communications) are likely to give population exposures below those encountered with either microwave ovens or mobile telephones. At present, GSM is the major source of outdoor emissions: whereas in remote rural areas TV and radio transmissions can represent up to 48% of overall irradiances, this falls to 13% in suburban/urban areas, and to 1% in inner cities (Hamnerius & Uddmar, 2000) where most of the population resides. Marine radar on small vessels may be a significant source of exposure as power densities immediately adjacent to the antennae can routinely exceed 1 mW/cm^2, but would only affect a small minority of the population.

Although mobile telephony is generally thought to afford the highest levels of exposure, one report has indicated that AM radio emissions can exceed other exposures, with a power density of 0.0464 microW/cm^2 being recorded from AM radio alone (ARPANSA, 2008). However, handset emissions were not measured in this study, the recording was from a single site in Victoria, and the irradiance was well below emissions recorded from handsets in other studies.

Estimates of Overall Exposures

In considering exposure levels and their potential contribution to neurodevelopmental effects there are many uncertainties. Individual usages and hence exposures inevitably will vary widely according to habit, profession, social stratum, geographic location and other factors. However, to provide a reference point for debate Table 1 overviews anticipated pre-natal exposures from microwave devices. The table has not been adjusted to allow for maternal shielding: penetration of biological tissues tends to diminish markedly over a few centimeters (e.g., Khalatbari, Sardari, Mirazaee, & Sadafi, 2006) and the figures probably overestimate actual exposure of the fetal nervous system. It is also assumed that the developing fetus and neonate are seldom if ever exposed to close mobile handset emissions, but parental use within

Table 1: Relative emission levels relevant to potential in utero and early postnatal exposures to microwave radiation

Source		Irradiance / Peak Irradiance (a) (microW/cm^2)	hrs/day	Relative Exposure
microwave oven	50 cm from source	50 (b)	0.07 (c)	0.35
mobile phone handset	10 cm from source	10 (d)	2.4 (e)	1
mobile phone handset	50 cm from source	0.4 (d)	2.4 (e)	0.04
cordless telephony (DECT/DHFSS) (f)	50 cm from source	20	12 (g)	10
cordless telephony (DECT/DFHSS) (f)	adjacent bedroom	0.65 (h)	12 (g)	0.33
mobile telephone mast	top 5%	0.1 (i)	24	0.1 (i)
mobile telephone mast	mean	0.01 (i)	24	0.01 (i)

(a) Does not consider shielding by maternal tissues.
(b) Rounded (maximum) figure; in the majority of cases exposures will be lower.
(c) Assumes exposure for 4 minutes per day: In a two week survey period maximum use was 77 minutes, when in use the microwave was most frequently used for a 2 min period, mean use was twice per day (DEFRA Market Transformation Programme 2006); maximum usage of 77 minutes equates to 5.5 minutes per day, average usage is fractionally lower. Percentage operator time spent adjacent to the appliance is not known.
(d) Mobile phone emissions: this assumes that maximum field intensities are generated continuously during active use, a probable over-estimate. Calculated from a legislated maximum field intensity of 1 mW/cm^2 at 1 cm distance.
(e) 10% usage (2.4 hours per day, all days) is a probable over-estimate.
(f) Based on a single report (Haumann & Sierck 2002).
(g) Assumes 50% occupancy.
(h) Mean figures from adjacent bedroom in a typical household (range: 0.07 to 1.4 microW/cm^2; maximum peak pulse value).
(i) Building structures absorb or reflect a large fraction of incident radiation; indoor exposures to mast/base-station emissions were reduced over outdoor exposure by a factor of 7.6 (Mann et al. 2000).

50 cm may be commonplace. The greatest irradiances of importance to neurodevelopmental toxicity are obtained from handsets and cordless base-stations, where power densities up to 1 microW/cm^2 are likely to be encountered routinely in the home. This substantially exceeds emissions from base-stations (0.01-0.1 microW/cm^2) (Table 1), particularly indoors where base-station signals are further reduced (approximately 8-fold; Mann et al., 2000).

Biological Effects of GHz Exposure: Reviews and Surveys

The primary effect of microwave radiation is to induce heating in exposed tissues; high intensity microwave exposure is predictably lethal as a result of hyperthermia. At lower intensities it is still unclear whether microwaves in the GHz range can induce biological effects beyond simple heating. The field has been comprehensively reviewed (Heynick, Johnston, & Mason, 2003; Leonard, Berteaud, & Bruyere, 1983; McRee 1972; Meltz 2003; Michaelson 1991; Stuchly 1979; Verschaeve & Maes 1998), and through independent surveys (Advisory Group on Non-Ionising Radiation, 2003; BioInitiative, 2007; Hennies, Neitzke, & Voigt, 2000; IPCS, 1981; Repacholi, 1998; WHO Evaluation Group, 1975), including the influential Stewart Report (IEGMP, 2000). Most commentaries point to insignificant risks of exposure to microwave radiation, but specific themes recur.

Ocular Effects

Experiments on the effects of microwave exposure on the eye date back to the 1940s. Principally conducted in rabbits, due to the similarity of the eye to the human organ, the minimum power density level at which cataracts were formed was approximately 150 mW/cm^2 for 100 min (IPCS, 1981). At lower doses no adverse ocular effects were observed. This energy level is far above any routinely encountered by human subjects, though cataracts have been reported in accidental exposure to high intensity microwave emissions (McRee, 1972). Cataract formation has been attributed directly to the thermal effects of microwave radiation.

Genotoxicity

Diverse reports have appeared suggesting that microwave exposure can induce potentially mutagenic

changes, including chromosome aberrations, DNA breakage and micronucleus formation, both in vivo and in vitro. However, several long term studies failed to substantiate such changes. For example, Vijayalaxmi, Sasser, Morris, Wilson, and Anderson (2003) exposed pregnant rats for 2 hours per day to a 1.6 GHz communication signal (0.43 mW/cm^2), followed by chronic exposure of offspring for 2 yr (1.6 GHz, 2 hours per day, 5 days per week). At the end of 2 years, bone marrow smears were examined for genotoxicity, assessed from the presence of micronuclei in polychromatic erythrocytes. There was no indication of any increase. Juutilainen, Heikkinen, Soikkeli, and Maki-Paakkanen (2007) exposed mice for up to 78 weeks (1.5 hours per day, 5 days per week) to a pulsed 902.4 MHz signal resembling the GSM output, and found no evidence for increased micronuclei in blood erythrocytes. Other regimens mimicking different types of mobile phone exposure were also negative.

In contrast to these studies, habitual mobile phone users may be at increased risk of brain tumors. For example, Hardell, Mild, Carlberg, and Hallquist (2004) reported that brain tumor incidence was elevated by a factor of 1.3 in users, the risk factor rising to over 5 when sub-groups were considered separately. The inference is that high-level irradiance in the immediate vicinity of the telephone handset may be responsible. Other reports have reiterated an increased risk of brain tumors (Berg et al., 2006; Kundi, Mild, Hardell, & Mattsson, 2004), but results have sometimes been inconsistent, with many studies limited by short follow-up periods and non-rigorous exclusion of confounding factors (Elwood, 2003). Nevertheless, the Interphone study, a trans-national survey of the association between mobile phone use and brain tumors (glioma, meningioma, acoustic neurinoma and parotid gland tumors), found that 8 of 10 studies comparing tumor risk on the ipsilateral side to that on the contralateral side reported excess ipsilateral tumor incidence (INTERPHONE, 2008). The potential link with brain tumor development provides a warning that mobile phones may not be health neutral.

Nervous System

Anecdotal accounts of perceptual signs in subjects exposed to mobile phone handset emissions include headache, fatigue, feelings of discomfort, warmth around the ear and difficulties in concentrating (McRee, 1972; Sandstrom, Wilen, Oftedal, & Hansson, 2001). These observations have not been thoroughly replicated. One possibility is that some individuals may have heightened sensitivity to microwave radiation.

A double-blind study employing a GSM mobile phone signal was unable to find any evidence in support of this contention (Rubin, Hahn, Everitt, Cleare, & Wessely, 2006): sham exposure was sufficient to trigger headache and other symptoms in some participants. The authors argued that these have an origin in psychological factors and were not attributable to microwave radiation. However, others have argued that the headache phenomenon is probably real (Frey, 1998) although provocation studies indicate that symptoms are not related to actual exposures to electric or magnetic fields (COMAR, 2002).

In experimental animals, principally rodents, diverse effects on behavior have been observed at high exposures (generally above 5 mW/cm^2) including alterations in activity and exploration, motor activities, and seizure thresholds. Nevertheless, most such effects may be thermally mediated (D'Andrea, Adair, & de Lorge, 2003), though non-thermal behavioral changes at lower exposures have not been excluded.

Other Effects

Commonly reported effects of microwave radiation include interference with immune and endocrine systems in exposed subjects, with circulatory effects including hypotension and bradycardia. These effects have not been widely confirmed at realistic exposures. It is of note that immune, inflammatory, endocrine and cardiac anomalies have sometimes been seen in association with ASD.

Low Intensity Radiation: Potential Mechanisms Relating to Childhood Neurological Disorders

Pathways through which microwave radiation might impinge on brain development and function are clearly relevant. Neurons fire typically at frequencies under 1 KHz, and emissions in the GHz range may be too rapid to interfere significantly with neuronal firing, but biological effects have been seen both in vitro and in vivo.

Blood-Brain Barrier

Oscar and Hawkins (1977) reported that exposure of rats to 1.3 GHz microwave radiation at less than 3.0 mW/cm^2 led to increased uptake of D-mannitol into the brain, and suggested that the radiation impairs the integrity of the blood-brain barrier (BBB). Although many other studies failed to repeat this finding (e.g., Finnie et al., 2002; Franke, Ringelstein, & Stogbauer, 2005; Ward & Ali, 1985), others have confirmed BBB effects. In a co-culture model irradiated at 1.8 GHz (Schirmacher et al., 2000) increased permeability to sucrose was seen. Salford, Brun, Eberhardt, Malmgren, and Persson (2003), using a genuine GSM mobile phone, exposed rats to power densities of 0.024-2.4 mW/cm^2.

Immunohistochemistry revealed albumin diffusion into brain tissue, from many small foci, representing leakage from the cerebral vasculature, with some neuronal death. Damage levels were similar at 0.24 and 2.4 mW/cm^2. Although it has been argued that BBB effects may be exclusively thermal in origin (Moriyama, Salcman, & Broadwell, 1991; Williams, Lu, Del Cerro, & Michaelson, 1984) the finding of albumin leakage at 0.24 mW/cm^2 (Salford et al., 2003), an irradiance that would be considered insufficient to cause significant heating, suggests that BBB impairment may be induced by microwave radiation at levels encountered by some mobile phone users.

BBB deficits and consequent brain damage have been linked with ASD development. The complex mechanism requires the conjunction of two factors. First, hepatic immaturity (common in neonates) predisposes to excesses of toxic heme-related blood pigments (as in jaundice). Second, perinatal oxygen starvation (due to birthing difficulties) results in failure of the BBB, permitting influx of pigments into key brain regions. This in turn causes kernicterus (yellow brain) and neuronal death, resulting in mental deficits similar to autism (see DeLong & Heinz, 1997; Paksoy, Koc, & Genc, 2004; Windle, 1963; Windle, 1969). On this basis, impaired BBB function in the peri-natal period would be a major risk factor for early-onset neurological disorders.

Calcium Channels, Apoptosis, and Reactive Oxygen Species

A recurrently-reported effect of microwave radiation concerns calcium release. Early studies pointed to calcium efflux in exposed chick cells (Bawin, Kaczmarek, & Adey, 1975). Cultured human neuroblastoma cells, irradiated at 915 MHz, released calcium into the culture medium (Dutta, Subramoniam, Ghosh, & Parshad, 1984; Dutta, Ghosh, & Blackman, 1989). Loss of calcium homeostasis can cause programmed cell death (apoptosis); some studies suggest that microwave radiation may induce apoptosis (Buttiglione et al., 2007). However, others failed to discern any changes in programmed cell death (Joubert et al., 2006; Merola et al., 2006) though induction of the Fas apoptosis pathway was seen in a human T-cell line (Peinnequin et al., 2000).

Changes in gene expression and activation of regulatory cascades have been investigated. No alterations in gene expression were seen in irradiated glioblastoma cells (Qutob et al., 2006) but upregulation of the *Egr-1* immediate early gene was observed in human neuroblastoma cells (Buttiglione et al., 2007). Microwave irradiation can induce the hsp27/p38MAPK stress pathway in human endothelial cells (Leszczynski et al. 2002). Friedman, Kraus, Hauptman, Schiff, and Seger (2007) attempted to delineate the pathway for the activation of mitogen-activated protein kinase (MAPK), and proposed that the primary target for microwave irradiation is the induction of reactive oxygen species through the induced action of NADH oxidase.

Although these reports suggest that microwaves may impinge directly on neuronal cell activation, it is unclear how the radiation dosages in these studies compare with those likely to be encountered in vivo. The range of effects is confusing: different studies report expression elevation for diverse genes, there has also been a tendency not to adjust for multiple comparisons. Even so, the overproduction of reactive oxygen species (Friedman et al., 2007) is notable because of established effects on neuronal survival (Andersen, 2004) and overlaps with ischemia, blood brain barrier disruption, calcium dysregulation and apoptosis.

Neurogenesis

The dentate gyrus of the hippocampus, a brain region implicated in the behavioral disturbances of ASD, is unusual in that it contains dividing cells even into adulthood. In young adult gerbils a 35 kHz electromagnetic field resulted in a reduction in cell proliferation rates (Hoffmann, Bagorda, Stevenson, & Teuchert-Noodt, 2001) but this finding has not been confirmed.

Neuronal Signaling in the Brain: Key Role of Low Frequency Modulation

Mobile telephone signals are not continuous GHz oscillations. Early systems were amplitude-modulated at low frequencies, while the now ubiquitous GSM signals are pulse modulated at 217 Hz. This is in a frequency range critical for brain development and function. 30-100 Hz oscillations are implicated in attention and memory processes in the human brain (Jensen, Kaiser, & Lachaux, 2007). 60-100 Hz oscillations are associated with the onset of epileptic seizures (Worrell et al., 2004) and 100-500 Hz discharges are commonly seen between seizure episodes (Urrestarazu, Chander, Dubeau, & Gotman, 2007).

Effects of stimulation in this frequency range are observed at the level of the synapse. In the hippocampus, a brain region implicated in ASD (DeLong, 1992; Lathe, 2006), stimulation at between 100 and 400 Hz (but not at 0.1 Hz) induces a long-lasting increase in synaptic efficacy known as long term potentiation (LTP) (Bliss & Lømo, 1973; Malenka & Bear, 2004), a process that may underlie both learning and developmental wiring of the nervous system. Increased synaptic transmission can promote seizure activity while global LTP induction

(through a protocol resembling electroconvulsive therapy) leads to memory impairment (Reid & Stewart, 1997).

It is therefore possible that 217 Hz pulsed stimulation will interfere with brain function. Calcium release induced in neonatal chick brain by 147 MHz irradiation was increased by amplitude modulation in the 3-25 Hz range, with an up to 20-fold increase at 16 Hz (Bawin et al. 1975). In neuroblastoma cells exposed to 915 MHz radiation, calcium efflux was critically dependent on amplitude modulation at 13-16 Hz and again at 57-60 Hz (Dutta et al., 1984, 1989). Human brain rhythms revealed by EEG (electroencephalogram) recording are disturbed by microwave radiation. 0.45 GHz microwaves, with field power density at the scalp of 0.16 mW/cm^2, pulse-modulated at 7-21 Hz, brought a 17% increase in the intensity of alpha waves (8 - 13 Hz) (Hinrikus, Bachmann, Lass, Tomson, & Tuulik, 2008). In volunteers exposed to a 0.9 GHz signal, the EEG rhythm in the 10.5-11 Hz range was increased (Regel et al., 2007) but no changes were observed when the signal was continuous wave; effects were only seen with the pulse-modulated signal.

Because synaptic plasticity and LTP-like processes are implicated in the establishment of wiring patterns in the developing nervous system, modulated telecommunication signals (if sufficiently intense) have the potential to interfere with brain development. Signal modulation in the 1-1000 Hz range may be detrimental to the brain: "*if modulation is biologically significant … the entire rationale for RF (radiofrequency) exposure guidelines would need revision*" (Foster & Repacholi, 2004, p.224).

Mechanisms: Can Brain Tissue Demodulate Low Frequency Microwave Radiation?

Consideration has been given to the possibility that brain tissue might be capable of signal demodulation: if such a mechanism exists this would increase the likelihood of a biological response to microwave radiation. This issue has been discussed at length by Challis (2005) who observed that biological membranes, particularly when exposed to low frequency (below 1 MHz) radiation, can respond with changes in the transmembrane voltage gradient large enough to give rise to nonlinear effects including rectification. No demodulation was seen at frequencies above 1 MHz, emphasizing the importance of low frequency pulse modulation of microwave signals.

Cell surface ion channels may contribute to demodulation: ligand-gated ion channels including neurotransmitter receptors tend to be selective in the direction of catalyzed ion transport. When exposed to an oscillating field it is likely (though as yet unproven) that some receptors may generate net ion flow either into or out of the cell. Furthermore, Chiabrera, Bianco, Moggia, and Kaufman (2000) used quantum modeling of ion-binding to proteins and reported that binding is strongly influenced by radio-frequency fields below guideline values. This would imply that ion channels (not restricted to neurotransmitter receptors) may respond to electromagnetic fields, possibly predisposing to selective cellular depolarization in phase with the modulation frequency.

Sheppard, Swicord, and Balzano (2008) revisited the possible routes by which biological tissue might respond to microwave emissions and suggested that most known mechanisms, with the possible exception of biochemical changes based on spin-correlated radical pairs, are of a magnitude insufficient to give rise to biological effects.

It is also important to note that because mobile handset emissions are typically pulse-modulated in the sub-MHz range, positive battery currents within the device (required for signal emission) will produce rectified electromagnetic fields where no demodulation is required. No comprehensive surveys of the strengths of such rectified fields have been reported. Linde and Mild (1997) measured the magnitude of pulsed magnetic fields in the vicinity of handsets. The maximum magnetic flux density was negligible although only 2 devices were tested and it is likely that field intensity will vary markedly according to the precise design of the handset. In another study the computed peak magnetic flux density exceeded the derived peak reference level of ICNIRP, but the authors pointed out that these meansurements are not valid indicators of exposure (Jokela, Puranen, & Sihvonen, 2004). In a study on 5 different handsets, no device exceeded ICNIRP limits at 217 Hz, but in harmonic ranges (433 Hz, 650 Hz, 867 Hz and 1083 Hz) up to 4 of 5 handsets narrowly exceeded limits (by a factor of up to 2.0) (Tuor, Ebert, Schuderer, & Kuster, 2005).

A Possible Receptor for Electromagnetic (Microwave) Radiation

The brain target(s) for sub-thermal microwave radiation are not known. Life arose in the absence of significant microwave exposure; there has been no evolutionary pressure for the development of a dedicated receptor. However, there are indications that microwave emissions might activate pathways sensitive to static magnetic fields.

In organisms responsive to magnetic fields, from bacteria to bees and birds, the sensory system is based on microcrystals of magnetite (Fe_30_4) or sometimes griegite (Fe_3S_4). Magnetite has been discovered in the human brain (Kirschvink, Kobayashi-Kirschvink, & Woodford, 1992; Schultheiss-Grassi, Wessiken, & Dobson, 1999);

magnetite (or maghemite) levels were higher in a brain tumor sample (menignioma) than in native hippocampus (Brem et al., 2006). Magnetic iron biominerals were also present in the majority of rat brain samples analyzed (Pardoe & Dobson, 1999) and was influenced by dietary iron uptake. The function (if any) of these particles in human brain is not known, but magnetite absorbs microwave radiation strongly at frequencies between 0.5 and 10 GHz through ferromagnetic resonance (Kirschvink, 1996) and external low frequency alternating fields will also induce mechanical oscillations in the particles (Kirschvink et al., 1992) and heating. Many neurotransmitter receptors are sensitive to mechanical stimuli including membrane stress and stretch; magnetite oscillations would provide a mechanism for direct modulation of neuronal activity.

There is uncertainty about whether microwave radiation pulse-modulated at low frequency can induce mechanical oscillation of magnetite crystals. Nevertheless, Dobson and St Pierre (1996) reported that very low frequency pulses from mobile phones in standby mode (2 Hz) can produce torque on magnetite particles (discussed by Challis, 2005); in addition, rectified battery emissions are likely to induce magnetite oscillations at the frequency of pulse modulation.

Static magnetism has also been reported to have marked effects on cultured cells. Brief exposure to a static field increased DNA binding of a transcription factor (AP1) in cultured hippocampal neurons (Hirai, Nakamichi, & Yoneda, 2002). Molecular techniques were employed to detect responsive genes in rat brain, and *Ntan1* (amidohydrolase for N-terminal asparagines, a component of a protein degradation pathway) was identified: *Ntan1* expression was increased three-fold 3 h following brief exposure to a static magnetic field (Hirai et al., 2006). No studies on oscillating electromagnetic fields were reported, but when fetal or neonatal mice were exposed to magnetic fields (100 mT, 2 h, 4 times/d), *Ntan* expression was upregulated in hippocampus; animals showed decreased locomotor activity (Goto et al., 2006).

The existence of magnetite and magnetism-responsive genes in the mammalian brain provides an intriguing suggestion that there may indeed be specific mechanisms that could mediate neurological effects of microwave radiation. Modulation of emissions from mobile and cordless communications in a key frequency range adds further weight to the possibility that microwave radiation might adversely affect brain development and function. Although no specific mechanism has yet been demonstrated by which microwave radiation might affect brain function, one many not conclude that no such mechanism exists. Therefore the hypothesis under consideration: that microwave exposure might adversely affect brain development and function (Kane, 2004), is considered to be plausible: i.e., the available data do not yet refute the hypothesis.

Exposure During Gestation: Experimental Animals

The developing brain is more sensitive than the mature organ; microwave radiation is a potential source of toxicity to the developing nervous system of the embryo, fetus, and young child (Kheifets, Repacholi, Saunders, & van Deventer, 2005). Epidemiologic studies relating to in utero exposures to microwave radiation have so far not revealed any obvious risk (Robert, 1999) but there have been suggestions that physiotherapists exposed professionally to microwave radiation during pregnancy may be at increased risk of miscarriage or low birth weights (Lerman, Jacubovich, & Green, 2001; Ouellet-Hellstrom & Stewart, 1993).

Toxicologic studies in animals can afford helpful indicators of likely consequences in human. Effects of GHz radiation have been investigated in several models. A drawback of some studies is that the experimental irradiances employed have been substantially above the anticipated exposure level; some early literature reports described experiments with irradiances exceeding 100 mW/cm^2. For the general public, sustained exposure to GHz radiation (even in habitual mobile phone users) is likely to be in the 0.01-1 mW/cm^2 range (Table 1): investigations employing compatible exposures warrant scrutiny regarding potential effects on human health.

There have been more than 20 investigations into the effects of gestational exposure of experimental animals, primarily rodents, to microwave radiation (Table 2). Some early studies employed rotating fields where confounds could not be excluded (Ossenkopp, Koltek, & Persinger, 1972; Persinger & Pear, 1972). Using a variety of irradiation regimens, frequencies, and cumulative exposures, roughly half of more recent studies have reported an adverse biological effect. These results are to be viewed with caution because of publication bias towards reports recording positive effects versus no-effect studies. There was no obvious relationship between intensity/duration of exposure and effect (Table 2). However, it is of note that the level of exposure permitted under ICNIRP guidelines (1 mW/cm^2) falls midway through the table and represents a level of irradiance above several reports where biological effects were found.

Regarding behavioural effects, only 6 studies (all in rodents) explored the later-life behavioral outcome of microwave exposure during gestation. There was a relationship between exposure and outcome (Table 3). At

Table 2: Gestational and neonatal exposure studies

Species	Microwave frequency (GHz)	Irradiance (mW /cm^2) *	Regimen	Cumulative exposure (mW hr/cm^2)	Parameter	Adverse effect	Reference
Rat	0.1-1.0	0.14	2 min/day; days 3-18	0.07	learning and activity	No	Cobb et al. (2000)
Rat	0.915	3	90 min exposure	4.5	utero-placental blood flow	Yes	Nakamura et al. (2003)
Rat	0.9	0.1	continuous	21.6	behavior	No	Bornhausen & Scheingraber (2000)
Rat	2.45	20	3 hr/day; days 4-20	102	white blood cell number	Yes	Galvin et al. (1983)
Mouse	37-60	8	2 hr/day; days 6-15	160	learning, memory, c-fos expression	Yes	Zhao et al. (2005)
Rat	0.002	10	3 hr/day; days 5-10	180	body mass and behavior	Yes	Galvin et al. (1986)
Mouse	0.9	13.2	1 hr/day	250.8	BBB vascular permeability	No	Finnie et al. (2006a)
Mouse	0.9	13.2	1 hr/day	250.8	brain c-fos expression	No	Finnie et al. (2006b)
Rat	2.45	10	neonatal rats, 7 hr/day, 5 days	350	cerebellar Purkinje cells	Yes	Albert & Sherif (1988)
Rat	9.4	5	continuous; days 1-7	840	brain BMP expression	Yes	Pyrpasopoulou et al. (2004)
Rat	0.1	10	21 hr/day; days 17-21	1050	cerebellar Purkinje cells	Yes	Albert et al. (1981b)
Mouse	2.45	3	continuous	1368	brain enzyme activity	No	Kubinyi et al. (1996)
Mouse	2.45	30	8 hr/day; days 6-15	2400	brain histology; AChE activity	No	Nawrot et al. (1985)
Chick	0.428	5.5	continuous	2640	embryolethality, teratogenicity	Yes	Saito et al. (1991)
Rat	2.45	20	continuous	5400	tissue weights	No	Jensh et al. (1983b)
Rat	2.45	20	continuous	5400	activity	Yes	Jensh et al. (1983a)
Rat	6	35	continuous	7560	behavior	Yes	Jensh (1984; 1997)
Rat	1.6	0.43	2 hr/day; then exposure of offspring over 2 years	large	genotoxicity	No	Vijayalaxmi et al. (2003)
Rat	1.6	5.28	2 hr/day from day 19 of gestation until fully developed	large	survival, weight	No	Anderson et al. (2004)
Rat	Mobile	ns	continuous	ns	micronucleus cytotoxicity	Yes	Ferreira et al. (2006)
Mouse	20 KHz	ns	continuous	ns	brain enzyme activities	Yes	Dimberg (1995)
Sq. monkey	2.45	10	3 hr/day, 5 d/week, and postnatally	ns	cerebellar Purkinje cells	No	Albert et al. (1981a)

* some irradiances specified in W/kg bodyweight were converted to mW/cm^2 by multiplying by 3.3, a rounded conversion factor provided by the mean of the specific absorption rates (rat) from three different types of polarization and two frequencies (900 MHz and 2 GHz) according to Durney, Massoudi, and Iskander (1986); Sq. monkey = squirrel monkey; na = not applicable; ns = not specified; BBB = blood-brain barrier; BMP = brain morphogenetic protein; AChE = acetyl cholinesterase.

higher exposures (equal or greater to 0.67 mW per hour per day/cm^2) adverse effects were reported on several parameters including learning, memory, and activity. But, in rats exposed constantly to 0.1 mW/cm^2 throughout gestation, a single in-depth study (Bornhausen & Scheingraber, 2000) recorded no detectable later-life cognitive impairments. The study details are as follows.

Wistar rats were continuously exposed during gestation

Table 3: Behavioural studies in rodents exposed prenatally to microwave radiation

Species	Frequency (GHz)	Modulation	Irradiance (mW/cm^2)	Regimen	Cumulative (hr exposure) (a)	Cumulative dose (mW hours $/cm^2$) (b)	Relative exposure per day vs continuous (mW hr/cm^2/day) (c)	Behavioral outcome	Effect	Reference
Rat	0.1-1	1000 Hz	0.14	2 min/day; days 3-18	0.5	0.07	0.001	no measurable cognitive deficits	No	Cobb et al. (2000)
Rat	0.9	217 Hz	0.1	continuous	216	21.6	0.1	no measurable cognitive deficits	No	Bornhausen & Scheingraber (2000)
Mouse	37-60	No	8	2 hr/day; days 6-15	20	160	0.67	impaired learning and memory	Yes	Zhao et al. (2005)
Rat	0.002	No	10	3 hr/day, days 5-10	18	180	1.3	lower endurance, longer latency in startle test	Yes	Galvin et al. (1986)
Rat	2.45	No	20	continuous	270	5400	20	increased activity	Yes	Jensh et al. (1983a)
Rat	6	No	35	continuous	216	7560	35	abnormal T-maze and open-field performances	Yes	Jensh (1984)

(a) The figure gives total hours exposure during the gestation period. For continuous exposures the gestation period is taken as 21 days for both mice and rats.
(b) = h exposure x intensity.
(c) Relative per day exposure is calculated as h exposure x intensity during the exposure period, i.e. {h/day (Regimen)/24} x intensity}.

to a 0.1 mW/cm^2 0.9 GHz signal, pulse modulated at 217 Hz (pulse width, 0.577 ms) designed to simulate the highest population exposure to GSM digital telephony emissions. Exposed and unexposed offspring (n=96 for each) were tested as young adults (11-12 weeks of age) on a series of food-rewarded lever pressing tests designed to measure both learning and motor abilities. The learning demand ("*difficulty*") was increased incrementally until alternating level-pressing strategies were required, driving the animals to "*their limits of capacity*" (Bornhausen & Scheingraber, 2000). There was strictly no difference, nor trend towards a difference, between the exposed and sham-exposed groups.

This finding argues against adverse effects of low-level GSM signals during gestation. There are some caveats. First, there was high performance variability between animals with individuals segregating into "learners" and "non-learners" in both exposed and control groups (Bornhausen & Scheingraber 2000). This variation is not uncommon (Lathe, 2004) and could potentially conceal small inter-group differences. Second, it is not clear whether the tests applied would have detected the social/language/repetitive triad of disturbances that are diagnostic of autism. However, because a majority of ASD subjects (but far from all) have impaired performance on tasks measuring attention, learning and coordination, the tests applied would have detected such impairments. Importantly, a comparable test protocol detected the subtle cognitive deficits induced by methyl mercury exposure during gestation (Bornhausen, Musch, & Greim, 1980).

At face value, continuous (24 hours) exposure to microwave radiation during gestation/pregnancy of 0.1 mW/cm^2 is insufficient to cause detectable behavioural alterations in progeny. It is unfortunate that only one low-dose negative study (Bornhausen & Scheingraber, 2000) has been reported at realistic levels of exposure; despite the robustness of the analysis it is unsatisfactory to base concrete conclusions on a single experimental report. At irradiances 7-fold higher some behavioural effects in offspring have been described (Zhao, Zhang, Yan, & Ma, 2005). However, this report is fraught with even greater uncertainties, as the original publication is in Chinese and no translation is currently available; experimental details are restricted to those given in the English language version of the online abstract.

With these major caveats in mind, fetal exposure from mobile handsets and cordless phones at an estimated irradiance of under 20 microW/cm^2 (Table 1) does appear to be below the level reported to cause later-life behavioural changes in rodents. The inference is that microwave radiation, at levels of exposure likely to be encountered during gestation and early life, is insufficient to produce later-life behavioural impairments in human.

Time Course of the Increase in ASD rates: Comparison with Microwave Exposure

Recorded rates of autism and autism spectrum disorders (ASDs) have increased markedly over the last decades, with now approximately 1% of younger children being affected in western industrialized nations. The rise continues (Schechter & Grether, 2008). Though greater awareness and better diagnosis may account for some of the rise, a real increase has been confirmed. The timing of the rise is of importance in assessing a possible causal contribution of electromagnetic radiation from domestic appliances including mobile phones and microwave ovens.

Rise in Autism Spectrum Disorders

The two most influential studies have been a large survey in California, the Byrd study (MIND Institute, 2002) and a systematic meta-analysis in 2004 of all earlier studies (Blaxill, 2004). The Byrd study pointed to a first increase in the 1981-1984 birth cohorts (Figure 1B) while Blaxill's meta-analysis pointed to a first rise in ASD in the USA and UK case numbers in birth cohorts of the early 1980s, with a more rapid climb prior to 1990 (Figure 1A).

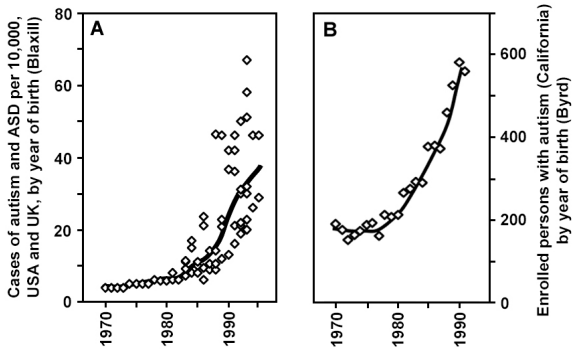

Figure 1: Rise in ASD case numbers by year of birth. A. Number of cases (autism and autism spectrum disorder) per 10,000 population, USA and UK; all single year point values according to year of birth (1970-1995) from figures 2 (a-d) of the meta-analysis of (Blaxill, 2004) were plotted (open diamonds) and a trendline added (solid line: moving average, Excel, Microsoft Corp., smoothed). B. Distribution of primary data concerning eligible cases (autism and pervasive developmental disorders) enrolled in the California Regional Center according to year of birth, data from the Byrd study (MIND Institute, 2002). Data were plotted and a trendline was added as before.

A further comprehensive survey confirms that ASD rates were already increasing by 1984, with suggestions that the trend may have commenced earlier (Newschaffer et al., 2005). An independent measure (the decline in representation of a specific genetic marker – Fragile X) demonstrates that rates were already rising in 1986 within birth cohorts of the early 1980s (Lathe, 2009). Other studies (not reviewed here) reiterate the same finding of a first rise in ASD rates associated with the early to mid years of the 1980s. Caution is needed in interpreting these data, as an exponential curve can appear to give different x-axis 'start-of-rise' points depending on the scaling of the y axis. Even so, the different sources of data agree that, until around 1980, ASD was extremely rare.

Microwave Ovens

Official statistics from the USA and Canada (Energy Information Administration, 2006; Statistics Canada, 2008) show the first introduction of microwaves in or before 1980, with a steep rise thereafter, followed by a near-plateau from 1990 (Figure 2).

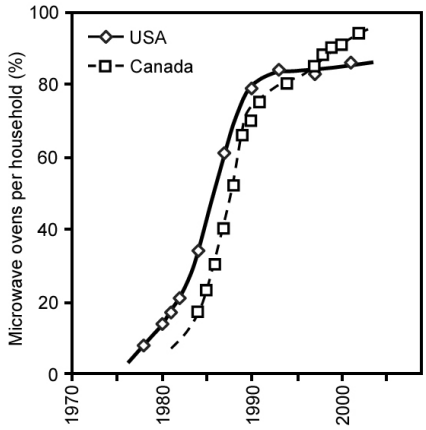

Figure 2: Microwave oven uptake in North America (Energy Information Administration 2006; Statistics Canada 2008).

In the UK, 55% of households contained a microwave oven by 1991, rising to 87% in 2002 (UK National Statistics, 2004).In Australia (Ironmonger, Lloyd-Smith, & Soupourmas, 2000) imports of microwave ovens show an approximately linear increase in cumulative number imported, with an intercept on the date axis at 1981 (Aitken & Ironmonger, 1996). The rise in domestic microwave usage is contemporary with the ASD rise. However, while microwave usage saturated in around 1990, ASD continues to rise, with the number of cases (6 years old, per 10,000 population) increasing from 11.5 to 24.1 between 1990 and 1994 (Newschaffer et al., 2005). Schechter and Grether (2008) report that California ASD

prevalence has risen from approximately 0.8 per thousand (6 years old, year of birth 1990) to 4.5 per thousand (year of birth 2000), a 5.6-fold increase. Over the same period there has been a change in microwave oven uptake of less than 15% (Figure 3). While the figure compares USA-wide microwave uptake to California ASD rates, the profile of microwave uptake in California is unlikely to have been slower than the USA mean. There is thus no strict equivalence between the rise in ASD and domestic microwave oven usage.

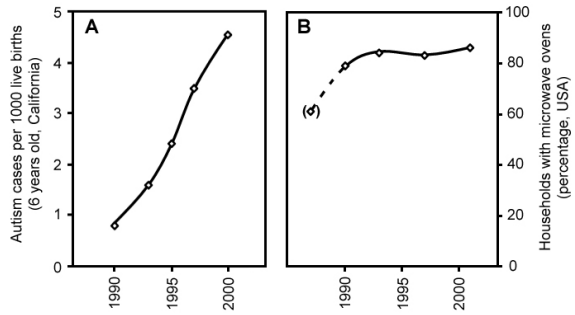

Figure 3: Ongoing increase in autism rates 1990-2000 versus plateau of microwave oven uptake. A: Autism rates among six-year old children recorded by the California Department of Developmental Services by date of birth (Schechter & Grether 2008). B: Uptake of microwave ovens in the USA, percentage of households with an appliance (Energy Information Administration 2006); the 1987 figure (in parentheses) indicates the rise prior to 1990.

Mobile Telephony

The rise in mobile phone use was later. The first commercial cellular network (NTT) was launched in Japan in 1979, followed by Europe and North America in the early 1980s. In the USA, in 1985, there were only 92,000 subscribers, rising steeply after 1995 to 250 million in 2007 (CTIA The Wireless Association, 2007; US Census Bureau, 2008) (Figure 4). In the UK, even as late as 1992 no more than 2 or 3 percent of the population had access to mobile phones, and the major rise in use only commenced in 1994, with the highest per year increase recorded in 1999-2000 (Mobile Operators Association UK, 2008). Worldwide, growth of mobile phone use in OECD countries has followed a similar pattern, with minimal uptake at 1990 followed by rapidly rising phone subscriber numbers, most acutely in 1997-1998 (National Science Foundation, 2002). The ASD rise therefore precedes by almost a decade the rise in mobile telecommunications that took place after 1990 and most steeply after 1995 (Figure 4).

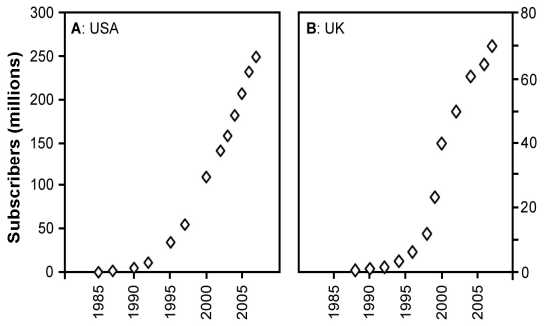

Figure 4: A: Mobile telephone subscribers in the USA according to year (CTIA The Wireless Association 2007; US Census Bureau 2008); B, subscribers in the UK (Mobile Operators Association UK 2008).

Domestic Cordless Telephones

These devices were first introduced in the early 1980s, but there was no significant uptake until about 1995, rising from under 5 million units shipped in 1996 to over 60 million in 2005 (DECT Web, 2007). In Canada, units shipped rose from over 2 million in 2002 to over 7 million in 2007 (Electrofederation Canada, 2006). Separate statistics for cordless and mobile phones are not available in the USA and UK, but it is presumed that there has been a steady (approximately linear) rise in the percent of households with cordless telephones from 1996 onwards. The timing is a decade later than the onset of the rise in ASD.

Discussion

Three approaches were used in this study to address the possibility that exposure to microwave radiation during gestation and the postnatal period might contribute to the rise in childhood autism as suggested (Kane, 2004).

First, plausibility was addressed through consideration of potential biological mechanisms have been considered. The unexpected presence of magnetite in human brain provides a possible mechanism by which microwave radiation might interfere with brain development and function. Furthermore, pulse-modulation of mobile and cordless telephone emissions is in a (sub-1 MHz) frequency band crucial for synaptic plasticity. There is some limited evidence indicating that microwave irradiation may compromise the blood-brain barrier, leading to neuronal apoptosis; this could overlap mechanistically with ASD risk factors. This observation is reinforced by many descriptions of bio-effects at low-intensity (sub-thermal) exposures, notably including the generation of neurotoxic reactive oxygen species. In the absence of contradictory data it is therefore plausible to

suggest that microwave radiation during gestation could potentially predispose to neurodevelopmental abnormalities in later life.

Second, studies employing exposure of rodents during gestation were analyzed. Here the power levels required to produce later behavioral deficits were above those likely to be encountered by the general population. Continuous gestational exposure to microwave radiation at 0.1 mW/cm^2 (100 microW/cm^2) was insufficient to cause detectable behavioral alterations in rodent progeny, while human fetal exposure from mobile handsets and cordless phones is unlikely to surpass 1-10 microW/cm^2. Even so, it is notable that the extrapolated exposure level causing adverse behavioral effects (continuous 0.67 mW/cm^2) was only marginally below the limit set by ICNIRP.

Third, the timing of the rise of ASDs was compared with the introduction of microwave ovens and mobile phones. ASDs began to increase in the early years of the 1980s. Microwave ovens were introduced around 1980, with a steep rise thereafter, but penetration reached a plateau from 1990 while ASD rates have continued to rise. The rise in mobile and cordless telephones took place after 1990 and most steeply after 1995, too late to explain the rise in ASD.

At face value, on the basis of these observations, it would appear that microwave radiation is unlikely to account for the ASD increase. There are, however, many uncertainties. An expert group observed: "*We were struck by certain inconsistencies and inadequacies in the scientific literature on the biological effects of RF (radiofrequency) radiation*" (IEGMP, 2000, p.47). Only limited data address the effects of microwave irradiation on brain development and function. The absence of behavioral changes in experimental animals subject to low-intensity (sub-thermal) irradiation during development depends on a single gestational (but not post-natal) study at realistic power densities. Other studies have used unrealistic exposures or employed unmodulated microwave signals: the potential impact of modulated (rather than continuous wave) beams is not to be underestimated (Foster & Repacholi, 2004).

No systematic retrospective studies have been performed in humans. Only one study has addressed a possible association between gestational microwave exposure and ASD development. It was recently reported that children (n=10) developing ASD appeared to have been exposed in utero to higher levels of electromagnetic radiation (median 20 microW/cm^2) than controls (median 1.4 microW/cm^2; n=5) (Klinghart, 2008). Nevertheless the sample sizes were small and statistical significance and potential confounds were not addressed.

The major limitations of our current knowledge-base have been recognized by the WHO (World Health Organization, 2006) whose stated high-priority research needs include investigations of the effects of exposure of immature animals to radiofrequency (RF) fields on the development and maturation of the central nervous system, to include prenatal and/or early postnatal exposure to RF fields.

The present analysis has inherent weaknesses. Because of their differing characteristics, exposures from mobile phones, cordless telephones, and microwave ovens were considered as independent factors. It is possible that if summated microwave emissions from all sources were to be considered a better fit with the rise of ASD might be obtained, although this has not been demonstrated. Microwave exposures have risen steadily from multiple sources not explicitly considered here, all with variable market penetration depending on geographical region, social strata and other factors. The available data do not permit even first estimates of combined exposures in typical western households, other than pointing to the conclusion that this is likely to be rising substantially.

At the same time, population exposure to environmental toxins of diverse types is generally increasing in all industrialized societies. Examples include heavy metals, preservatives and colorants, tap-water additives, and complex chemical toxicants such as dioxins and phthalates. Although observers increasingly agree that environmental agents continue to contribute to the rise in ASD, the primary causal factor(s) remain elusive. There has been a suggestive correlation between environmental exposure to diverse toxins including heavy metals (Windham et al., 2006) and elevated levels of porphyrins in the urines of children with ASD are suggestive of an environmental contribution (Nataf et al., 2006). However, in the latter study it is not known if porphyrin excess is as a result of heavy metal exposure or a marker of physiological stress.

The present analysis does not rule out dual exposure (for instance to both microwaves and another independent toxic influence) as a predisposing factor. Indeed, it has been suggested that microwave radiation might impair heavy metal clearance in ASD subjects (Mariea & Carlo, 2007) but this has not been confirmed. Conjoint risks warrant consideration because a combination of environmental toxins has the potential to cause more severe damage than any element in isolation.

A Need for Monitoring

Although the limits imposed by ICNIRP and other national and international authorities are generally in the range of 1 mW/cm^2 for general public exposure, this is generally calculated on a per-device basis. It is not

impossible that summated levels of exposure might exceed this limit. First, there is no systematic evaluation of manufacturer compliance and, because performance at distance improves with increased irradiance, there is an incentive to maximize power output. Second, with increasing uptake of electronic devices of all types it would not be uncommon to find exposures to microwaves from multiple independent sources in a typical western household. These sources include microwave ovens, mobile telephones and base-stations, hands-free telephone handsets, baby monitors, mobile computer wi-fi internet access, bluetooth technology. If each exposure is close to the ICNIRP limit, summated exposure is likely to exceed the limit by a large margin. There is therefore a clear need for official monitoring of device compliance and for routine surveillance of the ranges of exposures encountered across the spectrum of domestic households.

Conclusion

In the absence of firm data demonstrating that microwave radiation cannot influence brain tissue the contention that microwave radiation might contribute to the rise in ASD (Kane, 2004) is considered to be plausible. However, typical levels of domestic microwave exposure (e.g. up to 20 microW/cm^2 from mobile/cordless phone handsets and domestic base-stations) are below a level of exposure (continuous 100 microW/cm^2 during gestation) insufficient, in rodents, to cause lasting behavioral changes. Nevertheless, the safety margin (a factor of only 5-10) is clearly insufficient to warrant complacency. Indeed, on the basis of gestational data in animal models, it could be argued that ICNIRP guidelines may need to be revisited. Furthermore, the timing of the increase in ASD rates does not match the uptake of microwave ovens, mobile and cordless telephones. For this reason this analysis falls short of providing support for the contention that microwave radiation contributes to the rise in ASD. Nevertheless, it is not possible to refute the hypothesis based on the limited body of data available.

The present survey is offered as a first step towards evaluating the possibility that microwave radiation could contribute to ASD. To address the hypothesis rigorously, systematic analysis of routine exposures and how they evolve with time will be necessary, together with controlled studies into a possible association between microwave exposure and ASD development. As noted by the WHO, further studies into gestational exposure in animal models are required.

Evidence is emerging of other potential adverse effects of microwave radiation, and one remarks that autism is just one of several behavioral conditions whose prevalence is rising. It is now widely accepted that women during pregnancy should avoid a range of environmental hazards. The UK Stewart report advised restricting microwave exposure of young children (IEGMP 2000). This has now been mirrored by health authorities in France (see Reuters 2008). In the absence of further robust data on the effects of gestational/neonatal exposure to microwave radiation a precautionary approach would appear to be warranted (IEGMP, 2000), including the avoidance of excess microwave exposure of women during pregnancy. While the biological effects of microwave radiation warrant further investigation, vigilance by public health authorities is required to ensure that cumulative exposure does not inadvertently exceed regulatory limits. Routine precautionary surveillance of microwave-frequency exposures, particularly in inner-city locations, would appear to be justified.

Acknowledgements

The author acknowledges valuable comments and suggestions from K. Burns, M. Bornhausen, K. Foster, J. Hogg, L. Challis, and A. Philips.

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