



Health Effects Related to Radiofrequency Exposure

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BCCDC Grand Rounds

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Health effects related to RF exposure

Overview

- Basis for health concerns
- Background on RF
- Mechanistic approaches
- Electrohypersensitivity
- Brain activity
- Sperm as a target—infertility as an outcome?
- Brain, head and neck tumours
- Learning from exposed workers and patients
- Making sense of RF and health

Pre- and postnatal exposure to mobile phone use and behavioural problems in children

- Danish National Birth Cohort
- Recruitment in early pregnancy
- Behavioural status (*emotional, hyperactivity, conduct, peer relationships*), mother's pregnancy and postnatal mobile phone use, queried at child's age 7
- >13,000 respondents

Overall Behavioural Problems Score		
	Postnatal Exposure	
	No	Yes
Prenatal Exposure	95% CI OR	95% CI OR
No	reference	0.96 – 1.45
Yes	1.29 – 1.93	1.45 – 2.23
Postnatal Exposure	reference	1.01 – 1.38

Pre- and postnatal exposure to mobile phone use and behavioural problems in children

Overall Behavioural Problems Score					
<i>by prenatal and postnatal exposure (95% CI OR)</i>			<i>versus mobile phone use frequency</i>		
Covariates	Prenatal exposure only	Both prenatal and postnatal	Times Used /Day	#	OR (95% CI)
Boy	1.5 – 2.4	1.8 – 3.1	0 – 1	1873	reference
Girl	1.1 – 2.2	1.5 – 3.0	2 – 3	777	0.99 – 1.8
Socio-economic level			4+	347	1.02 – 2.2
• High	1.3 – 2.5	1.9 – 3.3	Missing	3258	
• Medium	1.4 – 2.5	1.4 – 2.6			
• Low	0.7 – 2.0	0.95 – 2.6			

“My name is Exxxx Gxxx and I presently live in Australia. I used cell phones for ten-plus years extensively on-and-off, and because of this I developed a brain tumour”

(May 20, 2008)



History of consumer use of RF in Canada

1920s/40s/50s


1980s

2000s

2010s



Expanding use of consumer RF devices

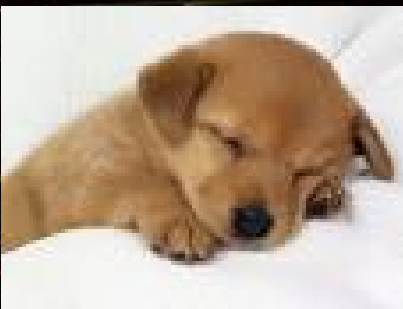
- 
- in ownership of mobile phones/smart phones
 - in frequency and duration of use
 - younger ages of first use (mobile phones and RF toys)
 - in use of WiFi or WLAN in homes, workplaces, schools
 - smart meter use – e.g. BC Hydro



Natural Sources



Biological Sources



RF is ubiquitous



Consumer Products




Industrial Sources




RF on the electromagnetic spectrum

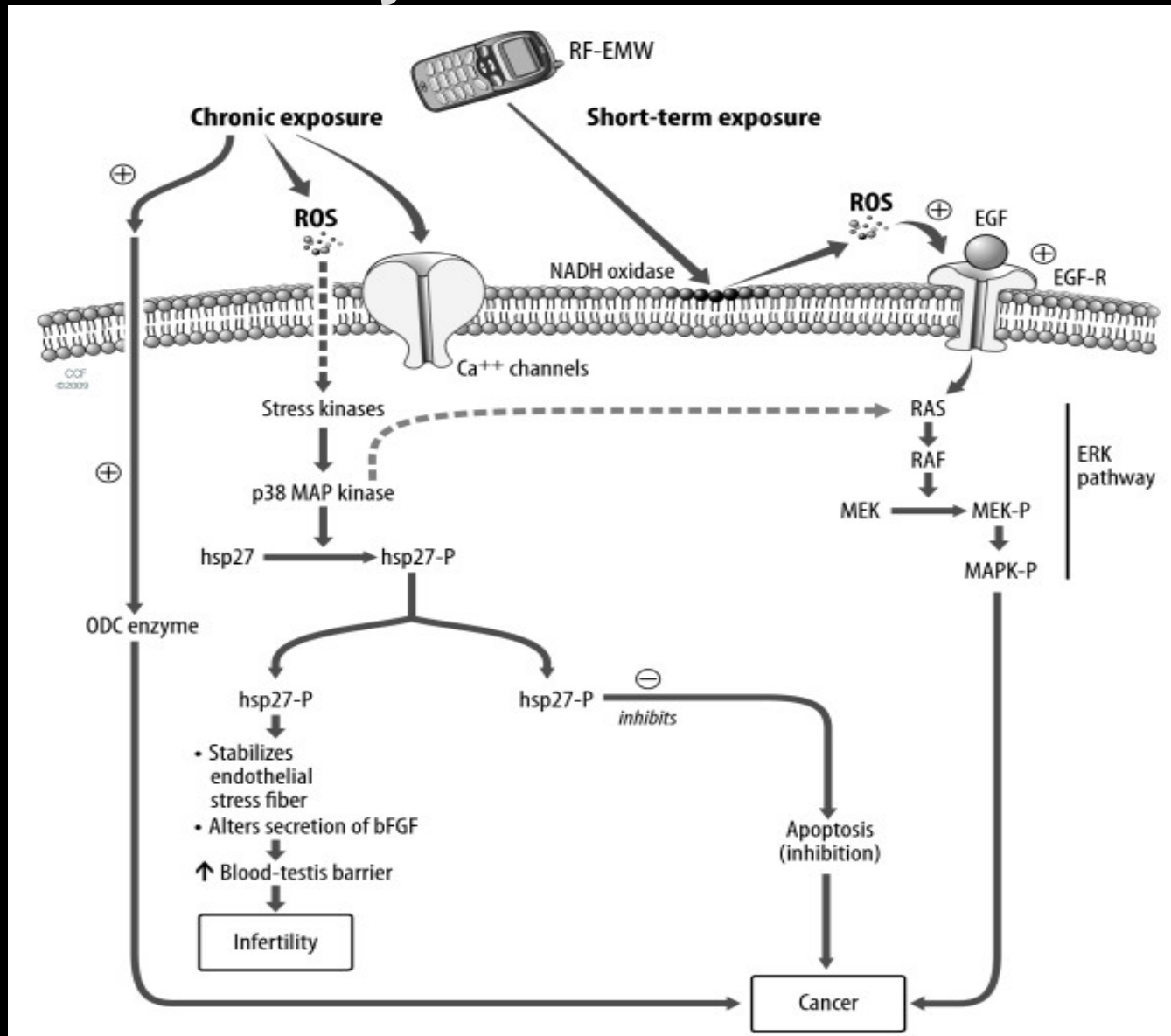
RF exposure characteristics

- 
- A black silhouette of a person's head and torso, facing right, holding a small white rectangular object (likely a mobile phone) to their ear with their right hand. The background is a light gray gradient.
- frequency (*or wavelength*)
 - intensity
 - duration
 - cumulative exposure
 - on/off characteristics
 - technology

Determinants of health effects

- 
- A black silhouette of a person's head and torso, facing right. The person's right arm is raised, with the index finger pointing towards the first item in the list. The background is a light gray gradient.
- exposure characteristics
 - proximity to source
 - tissue sensitivity
 - individual sensitivities
 - co-exposures

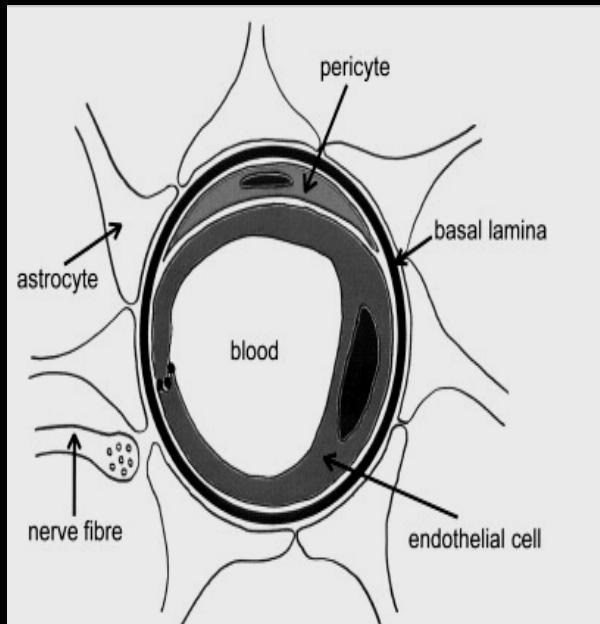
Suggested mechanisms of radiofrequency - induced infertility and cancer



Radiofrequency and the Blood-Brain Barrier

Studies on increased permeability of the brain-blood barrier:

- In-vivo studies on brains of small animals (rats, mice) (AGNIR, 2012).
- In-vitro studies: cultured rat brain cells (Wilhelm I, 2011; Zhou J X, 2013)
- Experimental conditions:
 - continuous and pulsed RF
 - low and high RF Specific Absorption Rates (SAR)
 - injection of dyes, drugs, radiopharmaceuticals to **test BBB permeability** (e.g., albumin extravasations)



Schematic of components of the blood–brain barrier (after Stam R, 2010)

- Most studies used **high exposure levels** (high SAR) resulting in thermal effects.

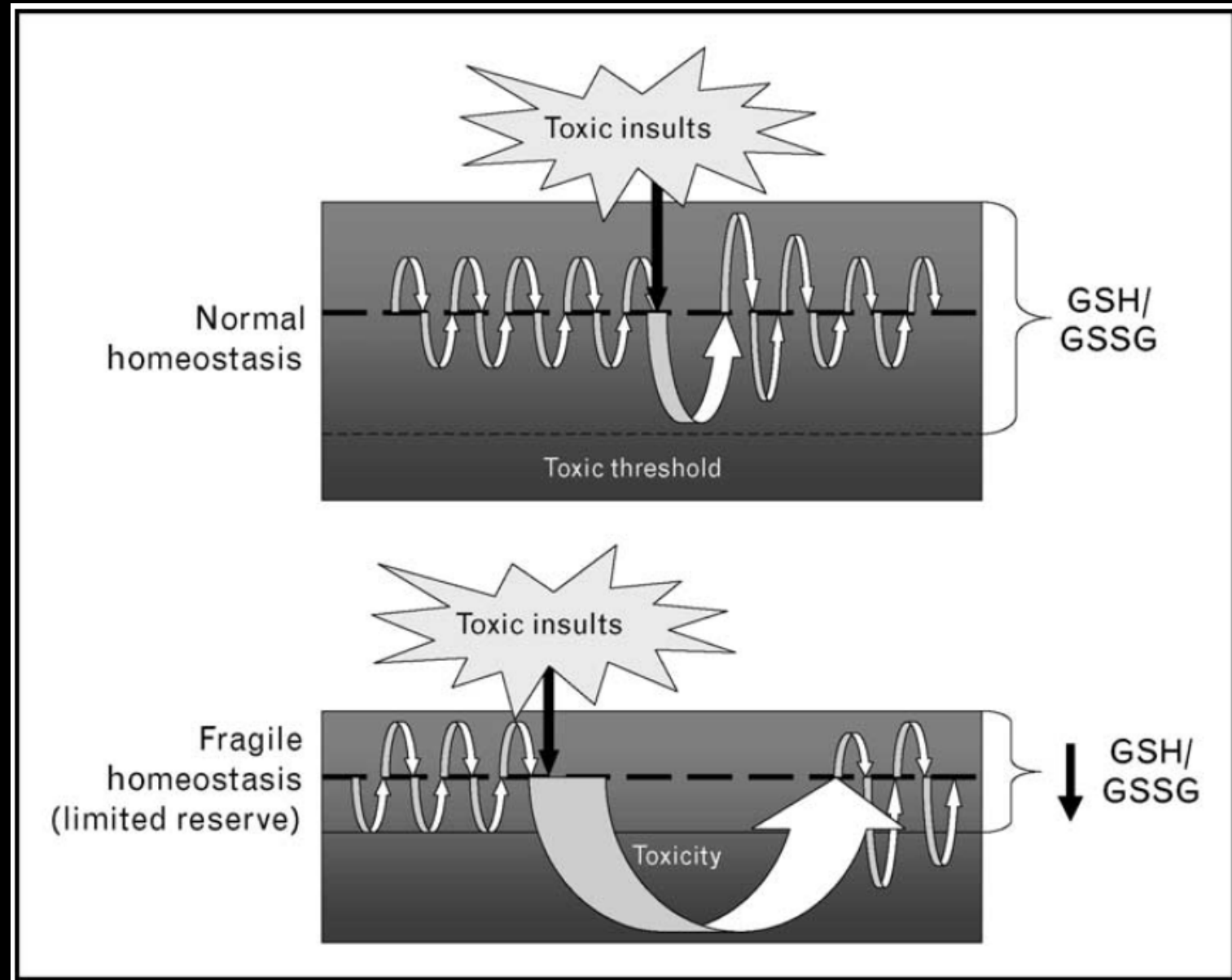
- Increased BBB permeability may have been a function of **higher than physiologic temperatures** (e.g. > 43 degrees) rather than a direct RF effect

- At non-thermal levels: studies that found increased permeability (temporary or permanent) were not replicated under the same exposure conditions

-Pulsed RF may be more effective at increasing the permeability of the BBB than continuous RF. Possible mechanisms advanced: increased cerebral blood flow, BBB cell shrinkage, increased ion mobility....

However, no such effects demonstrated at non-thermal RF levels.

Greater cytotoxicity from exposures can occur in the setting of impaired glutathione-dependent redox reserves



EHS cross-sectional studies: non-specific symptoms

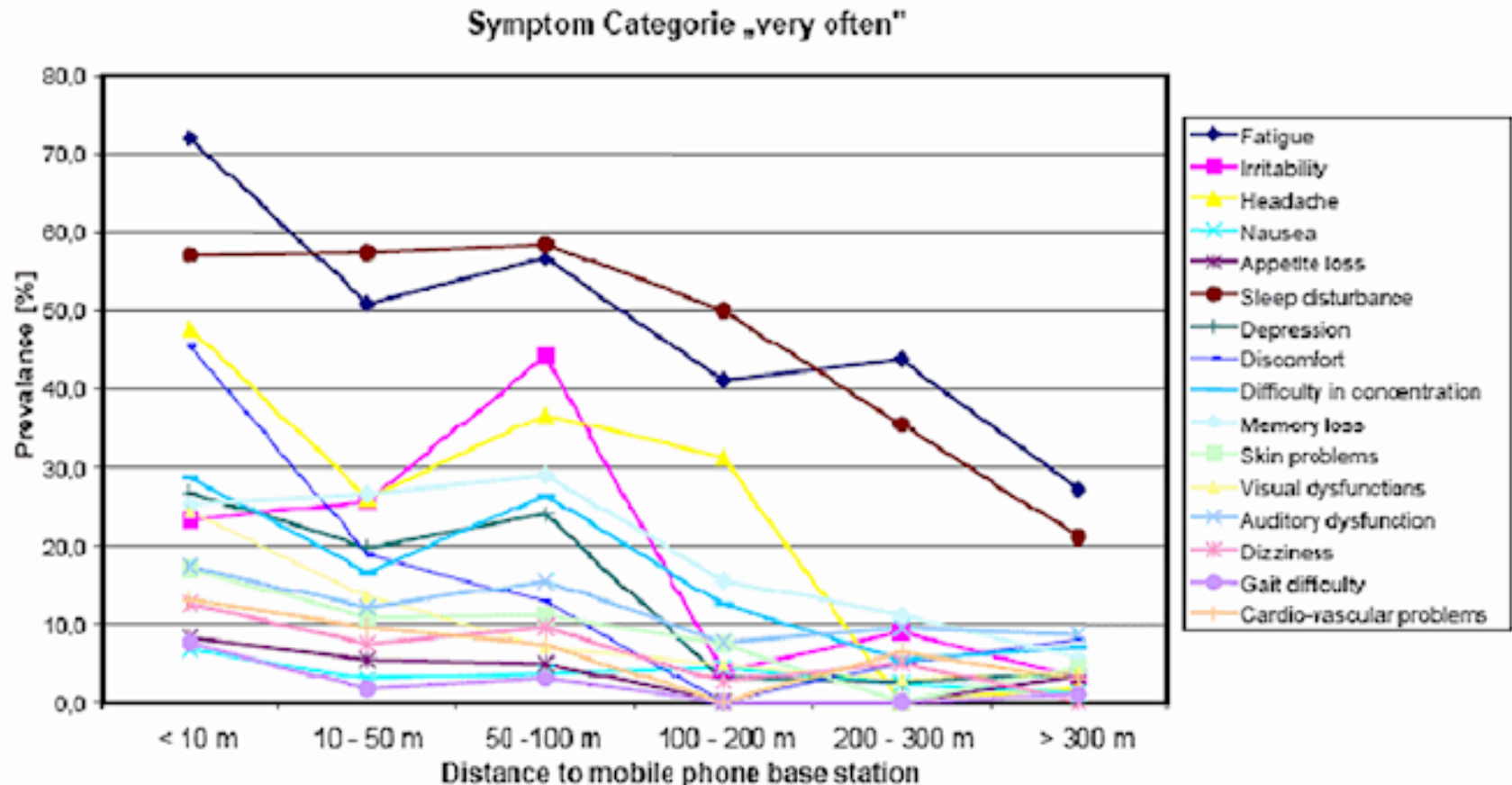
- Usual RF sources are mobile phone base stations
- Exposure = survey response, distance of residence from station, spot measurements in bedrooms or offices or personal dosimetry

Findings

- Mixed; more positive findings for perceived exposure rather than measured exposure to RF
- Studies of crude exposure measurements based on distance more often showed health effects, unlike that of more sophisticated measurements



Symptoms reported among persons living within 300 m of mobile base stations



Symptoms attributed to electromagnetic hypersensitivity syndrome (EHS)

Leitgeb, 2009

Abdominal pain	Headache	Numb limbs
Anxiety	Head pressure	Phosphenes
Appetite loss	Heart beat irregularity	Rash
Arousal decreased	Heart palpitation	Restlessness
Blood pressure increase	Hormonal disorder	Skin burning
Breathlessness	Hypersensitivity to medication	Skin redness
Chest pain	Hypersensitivity to noise	Skin tingling
Concentration difficulties	Intestinal trouble	Sleep disturbance
Crankiness	Irregular bowel movement	Stress
Daytime sleepiness	Irritation	Sweating
Digestive problems	Itching skin	Swollen eyes
Dizziness	Limb pain	Swollen joints
Dry skin	Metabolic disorder	Tachycardia
Exhaustion	Mood changes	Tenseness
Faintness	Mood depression	Tiredness
Fatigue	Muscle cramps	Toothache
Fear	Muscle pain	Trembling
Feebleness	Nausea	Unfeelingness
Feeling hot	Neck pain	Vision blurring
Forgetfulness	Neuralgia	Vomiting
Hair loss	Neurasthenia	Weariness

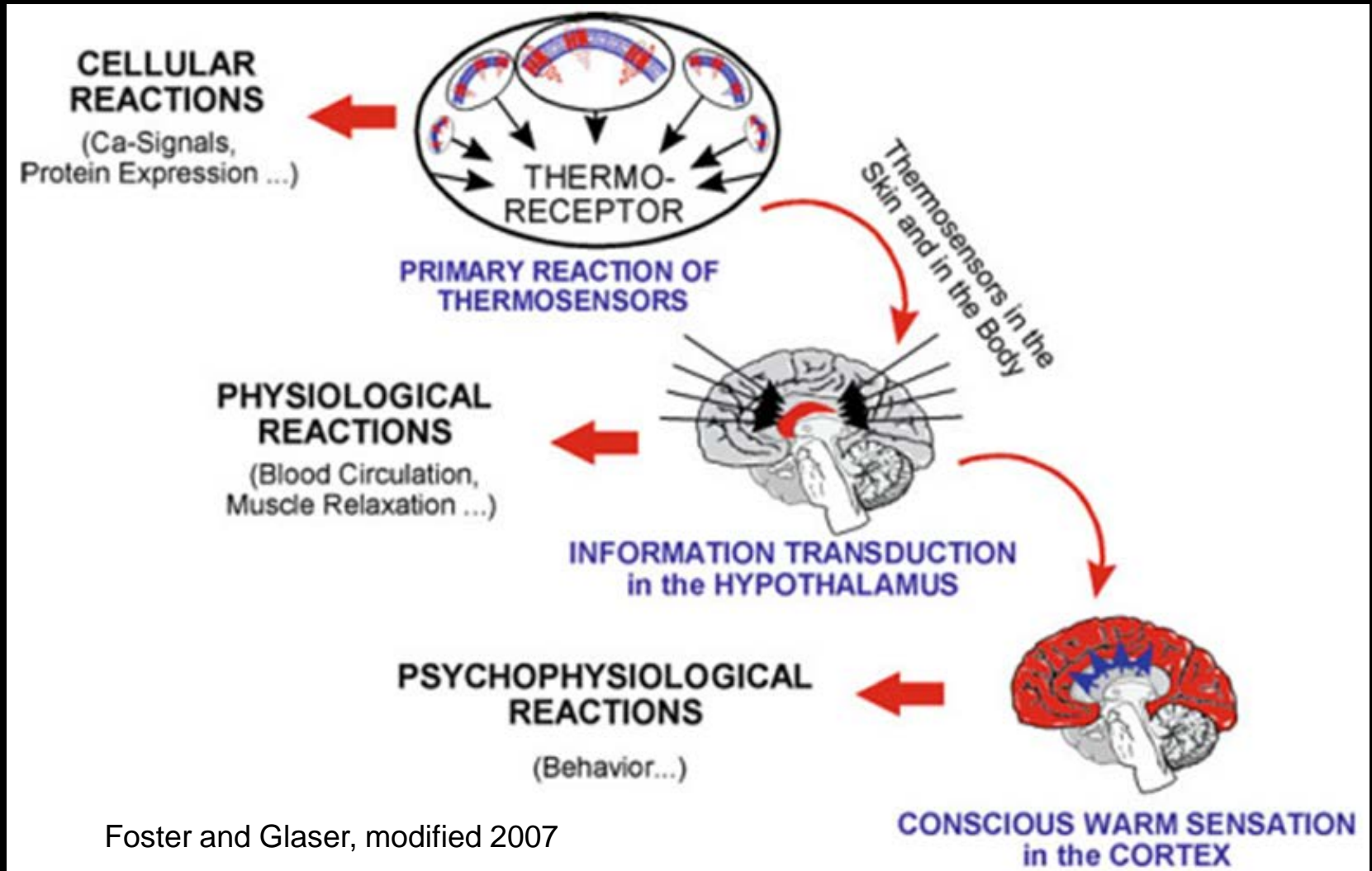
Electromagnetic Hypersensitivity Syndrome - EHS

Definition

- a collection of non-specific symptoms of varying degrees of severity that is attributed to environmental EMF
- not a recognized clinical syndrome although it can be debilitating
- also termed “IEI-EMF”
- estimated prevalence of EHS (2-10%)

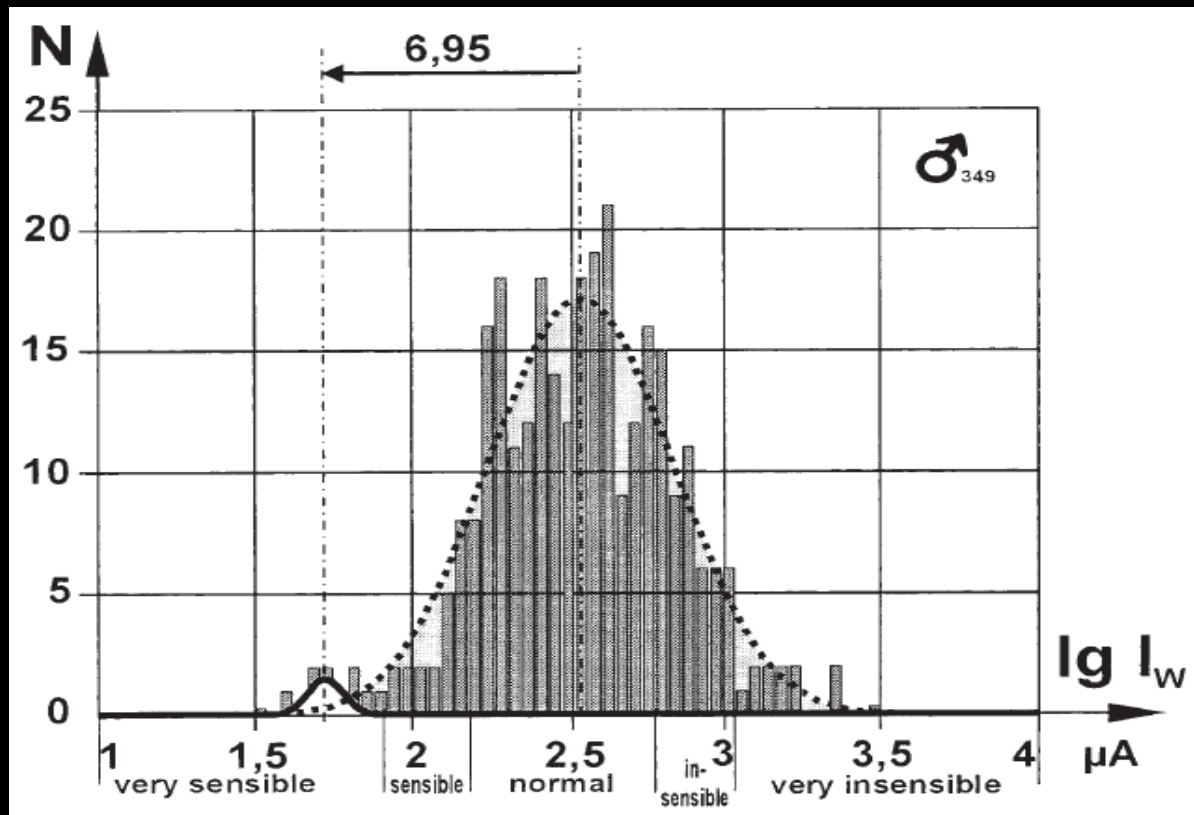


“Schematic illustration of the steps of thermosensation, starting from molecular reactions in thermoreceptor cells, up to the information center in the hypothalamus, leading in some conditions to conscious warm sensation”



Electrosensitivity

- Ability to **detect electric currents** – more EHS subjects have lower than general population perception thresholds
- Provocation studies with blinding show self-declared EHS subjects (*versus controls*) **could not reliably detect RF**

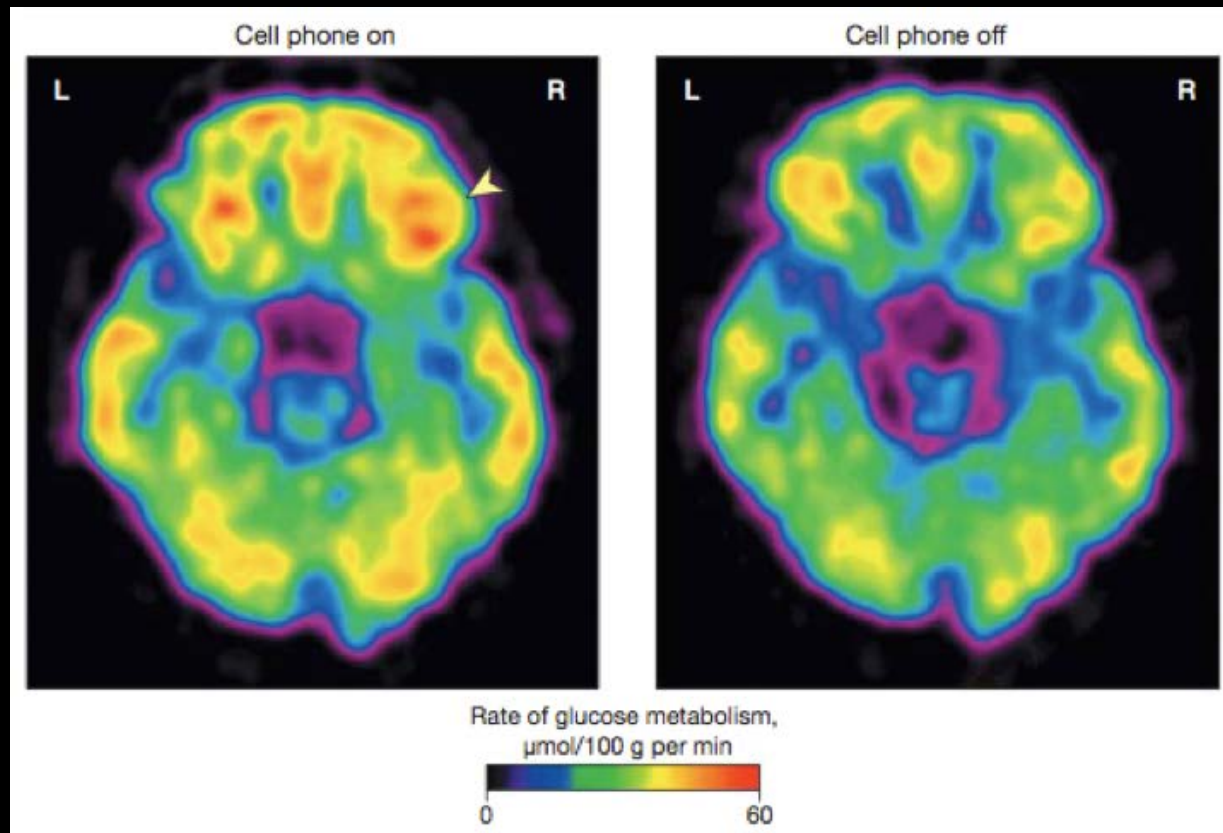


EHS – Nocebo effect

- 16 studies with measured RF from mobile phones (peak SARs ≤ 2 W/Kg) , base stations and magnetic fields (Rubin, 2010)
- EMF exposure **failed** to consistently and reliably trigger symptoms in EHS subjects
- **Nocebo effect** - symptoms occurring based on expectation rather than actual exposure
- but provocation studies are on acute symptoms only



Brain activity



PET image from a subject's brain. For the "Cell phone on" condition shown in the left part of the figure, only the cell phone on the right ear was active. The white arrow points to a red area of the image that indicates an increase in the rate of glucose metabolism in the area (right orbitofrontal cortex) near the antenna of the active cell phone.. In the "cell phone off" condition, much lower activity was noted.

Brain activity - importance



- Findings from EEG studies and newer studies of cerebral blood flow and volume are difficult to interpret.
- Do transient subtle effects in the laboratory setting imply health effects from long-term exposure to RF?
- E.g. Volkow (2011) concluded that *“in healthy participants and compared with no exposure, 50-minute mobile phone exposure was associated with increased brain glucose metabolism in the region closest to the antenna. This finding is of unknown clinical significance”*.

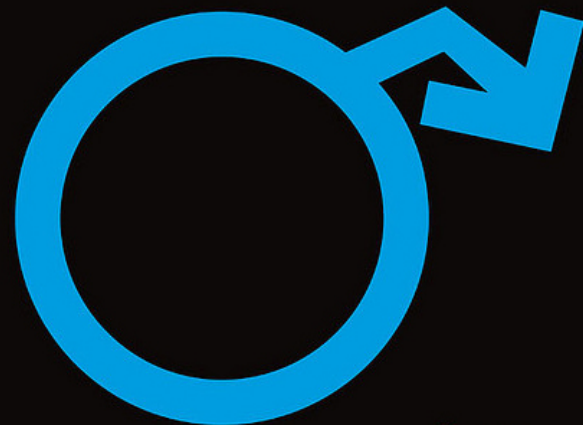
Infertility among male Norwegian naval officers

Work Type	<i>n</i>	% infertile	OR (CI 95%)
Telecommunications	24	15	1.04 – 2.85
Electronics	20	12	0.81 – 2.21
Radar/Sonar	17	17.5	1.27 – 4.09
<i>Unexposed</i>	<i>106</i>	<i>9</i>	<i>reference</i>

Møllerlækken and Moen, 2008

Male infertility – human studies

- Studies of infertility clinic patients consistently show decreased sperm mobility with use of mobile phones
- Exposing semen samples to RF from mobile phones generally results in a decrease in sperm motility

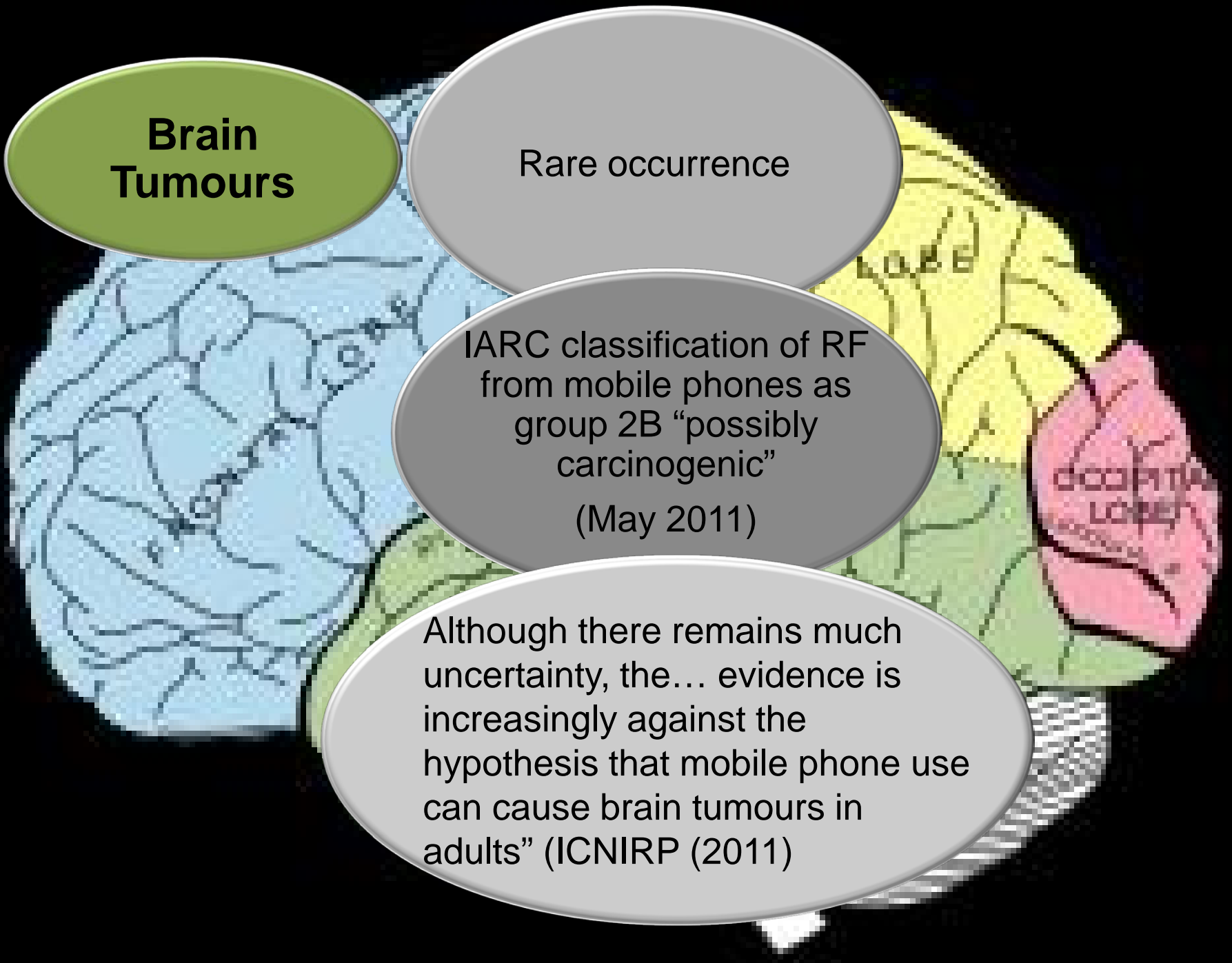


Researchers prove damage occurs in the mobility and DNA fragmentation of sperm if near the WiFi transmitter



24/07/2010 | Romina Martoglio. [From LaVoz.com](http://LaVoz.com)

“After four hours of incubation of sperm under the two different conditions, we found that in the sample exposed to the laptop, a large percentage of the sperm cells were affected,”



Brain Tumours

Rare occurrence

IARC classification of RF from mobile phones as group 2B “possibly carcinogenic” (May 2011)

Although there remains much uncertainty, the... evidence is increasingly against the hypothesis that mobile phone use can cause brain tumours in adults” (ICNIRP (2011)

Summary odds ratios of meta-analyses of **long-term** (and *ipsilateral*) use of mobile phones with ACOUSTIC NEUROMAS

Review	Long-term Use	#Studies	Summary Risk Estimate (CI 95%)*	Significant Individual Studies
Levis (2011)	≥ 10- yrs use & ipsilateral	3	1.2 - 2.6	Hardell (2008); Lonn (2004)
Repacholi (2011)	≥ 10- yrs use or cumulative	4	0.74 - 2.5	All NS
Hardell (2009)	≥ 10- yrs use and ipsilateral	4 3	0.97 - 1.9 1.1 - 2.4	Hardell (2006b) Lonn (2004) ipsilateral
Hardell (2008)	≥ 10- yrs use & ipsilateral	3	1.1 - 5.3	Hardell (2006b) Lonn (2004)

NS: Study risk estimates were not statistically significant

Summary odds ratios from meta-analyses of **long-term** (*and ipsilateral*) use of mobile phones with MENINGIOMAS

Review	Long-term Use	#Studies	Summary Risk Estimate (CI 95%)	Significant Individual Studies
Levis (2011)	≥ 10- yrs use & ipsilateral	3	0.9 - 1.8	All NS
Repacholi (2011)	≥ 10- yrs use or cumulative	2	0.5 - 3.1	Hardell (2005) analog
Hardell (2009)	≥ 10- yrs use and ipsilateral	5	0.8 - 1.4	All NS
		3	0.9 - 1.8	
Hardell (2008)	≥ 10- yrs use and ipsilateral	4	0.9 - 1.8	All NS
		2	0.99 - 3.1	All NS

NS: study risk estimates were not statistically significant

Summary odds ratios from meta-analyses of **long-term** (*and ipsilateral*) use of mobile phones with GLIOMAS

Review	Long-term Use	#Studies	Summary Risk Estimate(CI 95%) *	Significant Individual Studies
Levis (2011)	≥ 10- yrs use & ipsilateral	4	1.2 - 2.0	Hardell (2008) Lakhola (2007)
Repacholi (2011)	≥ 10- yrs use or cumulative	5	0.8 - 2.3	Hardell (2006b, 2010)
Ahlbom (2009)	≥ 6- yrs use	12	0.8 - 1.4	Hardell (2006a, 2006b)
Hardell (2009)	≥ 10- yrs use and ipsilateral	6 4	1.1 - 1.6 1.4 - 2.4	Hardell (2006a) Lakhola (2006)
Kundi (2009)	> 4 yrs & Ipsilateral	3	1.2 - 1.8	Hepworth (2006) Lahkola (2007) Hardell (2006b)
Hardell (2008)	≥ 10- yrs use and ipsilateral	6 5	0.8 - 1.9 1.2 - 3.4	Hardell (2006a,b) Lahkola (2005) (ipsilateral)

INTERPHONE study (2010)

IARC initiated a large international multi-center case control study (2,708 cases of glioma)

A significant reduced risk of glioma was found in regular users vs. occasional or non-users

For the highest decile of cumulative call time (>1640 hours of use) OR was 1.4 (95% CI 1.03-1.9).

Conclusion: "Biases and errors limit the strength of the conclusion we can draw from these analyses and prevent a causal interpretation".

Two major pooled case-control studies of GLIOMA compared: INTERPHONE (2010) versus **Hardell** (2011)

Design/Methods	INTERPHONE	Hardell
Place	13 countries	Sweden
Subjects' ages	30-59	20-80
Participation	64%	80-90%
RF exposure exclusions	hands-free devices	hands-free devices, DECT phones (separate analysis)
Questionnaire administration	face-to-face	mail-out, some phone follow-up
Exposure assessment	non blind interview	blinded, questionnaire based
Type of tumour	glioma	glioma,astrocytoma, oligodendroglioma
First use ≥ 10 yrs for glioma	~15% cases	~21% cases
Adjusted risk estimates	sex, age, study centre, education, ethnicity (Israel)	sex, age, occupation code, year of diagnosis

“Based on epidemiological studies there is a consistent pattern of increased risk for glioma and acoustic neuroma associated with use of mobile phones and cordless phones. The evidence comes mainly from two study centres, the Hardell group in Sweden and the Interphone Study Group. No consistent pattern of an increased risk is seen for meningioma. The different risk pattern for tumor type strengthens the findings regarding glioma and acoustic neuroma. Supportive evidence comes also from anatomical localisation of the tumor to the most exposed area of the brain, cumulative exposure in hours and latency time that all add to the biological relevance of an increased risk. In addition risk calculations based on estimated absorbed dose give strength to the findings.

Hardell, 2012

Case-control studies

As brain tumours are rare, case-control studies are practical

Limitations

- exposure misclassification
- selection bias should controls have a lower participation rate
- differential recall (cases may have stopped phone use due to symptoms)
- recall bias: over-reporting phone use on side of head where tumour occurred



Cohort studies

Meningiomas and Gliomas

- retrospective study of 350,000 Danish mobile phone subscribers found no evidence of increased risks of glioma and meningioma (Frei et al., 2011)

Limitations

- mobile phone subscriptions are not equivalent to actual mobile phone use
- accurate exposure assessment is affected by technology used, use of hands-free devices and multiple RF exposures

COSMOS

- European multicentre prospective cohort study; with plans to follow 250,000 adults over next 20-30 years (Schuz, 2011)

Occupational exposure studies

Occupational exposure limits - designed to prevent thermal effects and RF-induced contact shocks

MRI

chronic effects not seen in patients and operators



RF ablation

no studies on occupational health risks




Shortwave diathermy

no studies on adverse effects to patients



Strength of evidence assessments of health effects of weak RF fields in four recent reviews



Health Outcomes	None	Inadequate	Limited	Sufficient
Brain tumours in adults		UK Norway	Euro HRA	BIOINITIATIVE
Other cancers	UK Norway	Euro HRA		BIOINITIATIVE (EMF)
Neurocognitive effects/diseases	Norway (disease/performance)	Euro HRA	UK (EEG)	BIOINITIATIVE
Male infertility		Euro HRA	UK Norway BIOINITIATIVE	
Cardiovascular disease	UK Norway	Euro HRA		
Electromagnetic hypersensitivity syndrome	Euro HRA UK Norway			

UK Advisory Group on Non-Ionizing Radiation (UK, 2012)

Euro HRA European Health Risk Assessment Network on EMF exposure (2012)

Norway Norwegian Institute of Health Expert Committee (2012)

BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Radiation (2012)

Low prior + frightening implications = inflammatory epidemiology?

Pre- and postnatal exposure to mobile phone use and behavioural problems in children

Divan, 2008

- ubiquitous agent
- recently introduced
- incomprehensible workings
- common, dreaded outcome – child behavioural disorders

but

- low prior probability
- low energy deposition far from foetus
- multiple behavioural problems assessed (*emotional, hyperactivity, conduct, peer*) , none significant by itself
- parental report, potential recall bias

Savitz, 2008

Health concerns (bases)

- Longer-term, higher intensity use of older generation mobile phones and gliomas (epidemiology)
- Occupational exposures?
- Pants pocket mobile phones and sluggish sperm (experimentation)
- Baby monitors and mobile phone use by children (analogy)
- Ubiquity of exposure???



Making sense of RF and health

- Ubiquity of sources
- Ever-evolving technology---epi studies are of old technology
- Multiple attributes of exposure
- Hard to separate thermal effects
- Mechanisms in search of disease
- Appropriateness of animal models
- Long latency for many postulated outcomes, lack of case-definitions for others
- Need for multi-disciplinary approaches
- Politicization of the debate

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Thank You



Questions?
Comments?

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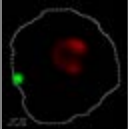



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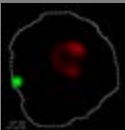



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