

 THE
NOTEBOOKS
OF THE
RESEARCH
health, environment, work

Radiofrequencies and health

Understand where the research stands

May 2021

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anses

ANSES and the health effects of radiofrequencies

The development of communications technologies translates into a wide variety of objects connected devices and wireless services using radio frequencies: baby monitors, security cameras, security, headphones, glasses, watches, key rings, blood pressure monitors... This exponential growth is not without raising questions that are the subject of permanent news both from a scientific and regulatory point of view and from a political and political point of view. societal. The growth in uses is likely to increase the exposure of the general population *via* new fixed transmitters, new mobile equipment or new uses (e.g. equipment worn close to the body, even inside the body or even the skin).

For several years, ANSES has been involved in expert appraisal activities in almost all areas of the non-ionizing electromagnetic spectrum: from extremely low frequencies to millimeter waves. With regard to the deployment of 5G technologies, the Agency collaborated with the ANFR to collect the first public exposure measurements taken before and after the commissioning of 5G on 1,500 sites located in France. In addition, from 20 April to 1 June 2021, it carried out an open consultation during which citizens could make contributions and comments on the expert report published in April 2021. Hence ANSES's updated opinion of February 2022 supported by an expert report supplemented and enriched with new data.

In view of the rapid evolution of technologies which leads to the exploitation of new frequency bands (such as those of 3.5 GHz and 26 GHz for 5G, in France), it seems essential, on the one hand, to adapt the methodologies for measuring and evaluating exposure and, on the other hand, to study the biological and health effects of electromagnetic waves in these frequency bands. To date, the number of users and 5G traffic are still limited in France in the 3.5 GHz band, while the 26 GHz band is not yet exploited by mobile telephone operators. ANSES's mission is part of a developing context and the data available in the literature are still scarce.

To estimate the impact of 5G technologies on health and the environment, the Agency regularly continues its scientific monitoring and updating work. Following the recent production of numerous data from new mechanistic studies, but also from epidemiological studies such as *Mobi-kids* (December 2021) or the key study of the "National Toxicology Program" (August 2020) on the development of tumors in rodents exposed to mobile telephone signals, an expert appraisal examining the carcinogenic effects of radiofrequencies is underway at ANSES, all frequency bands combined.

Finally, ANSES invests in the production of new scientific knowledge by supporting research on the health effects of radiofrequencies. This *Cahier de la recherche* presents eleven projects funded between 2017 and 2020 via the call for research projects

“radiofrequencies and health” of the national environment-health-work research program (PNR EST). So-called exploratory investigation projects (PIE) also make it possible to acquire new knowledge in response to questions raised by civil society, for example on the symptoms declared near relay antennas, hypersensitivity to electromagnetic fields or even the exposure to new mobile telecommunications signals including 5G. The need for this type of project was identified thanks to the dialogue initiated since 2011 with associative or professional stakeholders within the framework of the “Radiofrequency and health” dialogue committee.

Professor Benoit VALLET

Director General, ANSES

Research notebooks RADIO FREQUENCY AND HEALTH		#20
11	36	2.37
Projects valued	Research teams involved	Million euros allocated

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Warning to readers

The presentations of the research projects reflect the points of view of the partner scientific teams and do not commit either the supervising Ministries or ANSES and the associated partners. For any questions, the contacts are indicated at the top of each article.

General Introduction

Since the invention of the string telephone in 1665, various devices have been devised to be able to transmit and receive *the human voice at a distance* : from the "conversation pipes" of Jeremy Bentham (1748-1832)¹ to the telephone devices of Antonio Meucci (1849), Johann Philipp Reis (1859), Alexander Graham Bell and Elisha Gray (1876). To operate over long distances, these devices required an infrastructure or network of electrical wires that mainly followed railway tracks. In the United States, the first public line was operated in 1880 between Boston (Massachusetts) and Providence (Rhode Island). In France, a first line was launched in 1879 before being deployed in major French cities.² At that time, the invention of the telegraph, we were able to transmit visual³ or sound messages⁴ but in no manner of articulate voice.

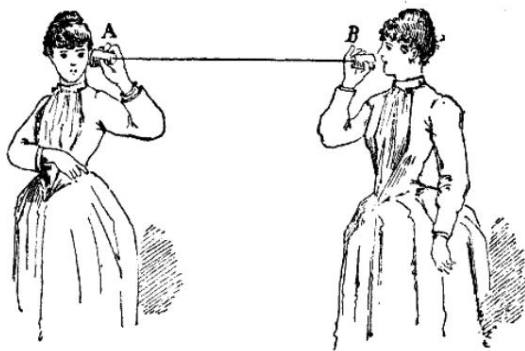


Figure 1: Hooke's Acoustic Telephone

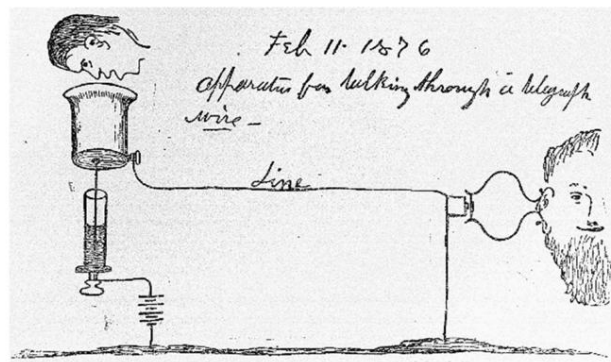


Figure 2: First phone diagram (Elisha Gray)

How do I chat remotely? "I wondered, for example, if speech itself could not be transmitted by electricity (...) The thing is practicable" wrote Charles Bourseul⁵ in 1854. Here is how: the sound of the voice makes a membrane vibrate connected to a magnet, which (by vibrating in turn) produces electrical impulses. These pulses are then transmitted by electrical wires (conductors) to the receiver. And vice versa.

For lack of research funds, the French scientist could not continue his work. This is how Alexander Graham Bell, while working with his assistant⁶ on a prototype harmonic telegraph, succeeded for the first time in 1876 in transmitting the human voice using electricity.

Radio or Hertzian waves

Ten years later, Heinrich Hertz noticed during an experiment that the discharge of a small emitter produces sparks on a nearby coil. He tried to reproduce this new phenomenon on several occasions, systematically bringing transmitter and receiver closer together. It worked: at a distance of two meters, the receiver also emitted electric shocks, confirming according to the

¹ For internal communication in its panoptic prison projects.

² In 1912, there was 1 telephone for every 183 inhabitants.

³ Optical telegraph by Claude Chappe (1794).

⁴ Morse code (1832).

⁵ Charles Bourseul, extract from the press article published in *L'illustration* of August 26, 1854.

⁶ Thomas A. Watson.

physicist *the laws of electromagnetism*⁷ : "We just have these mysterious electromagnetic waves that we can't see with the naked eye. But they are there. »

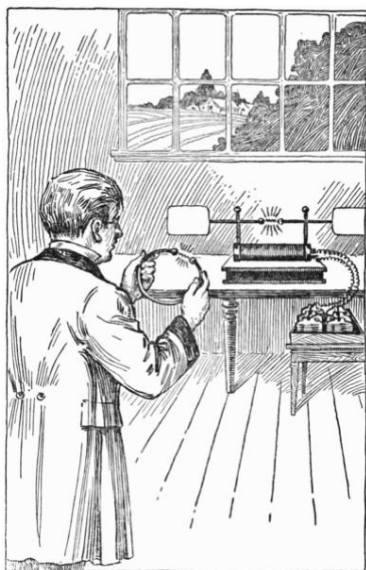


Figure 3: The Hertz experiment (1886)



Illustration 4: The theatrophone (poster by Jules Chéret, 1896)

Thus, electromagnetic radiation manifests itself in the form of an electric field coupled with a magnetic field. It propagates in the form of small waves (or oscillations), a bit like a wave on the surface of the water after having thrown an electric magnetic pole in it. To convince of the existence of waves Hertz multiplied the experiments⁹ engaged in hard work until his death, January 1, 1894. He had no idea that his discovery would be the basis of a large number of inventions such as the radio.

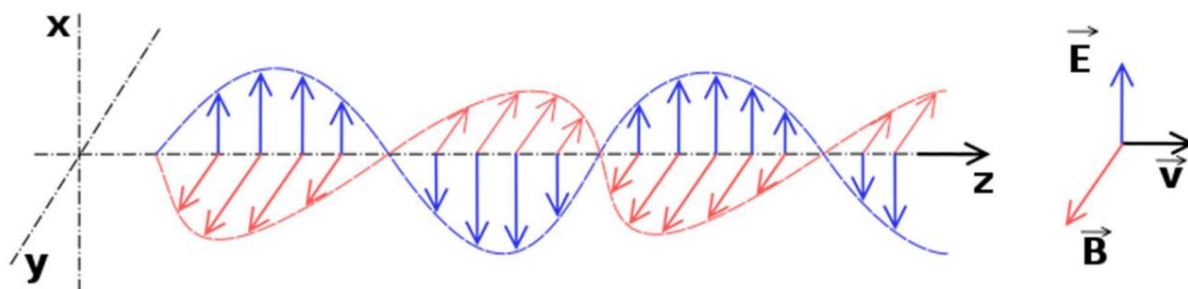


Figure 5: Electromagnetic wave, coupled oscillation of electric field (E) and magnetic field (B)

The Italian Guglielmo Marconi continued his work in 1895 by trying to improve them with the use of new materials: radio conductor (coherer) by Édouard Branly, antenna by Alexandre Popov... So much so that he carried out the first transatlantic radio transmission between the island of Newfoundland (Canada) and the county of Cornwall (England) in 1901.

⁷ Theory of James Maxwell according to which "light and magnetism are two phenomena of the same nature and that light is an electromagnetic disturbance propagating in space according to the laws of electromagnetism" (A *dynamical theory of the Electromagnetic Field*, 1864).

⁸ For the record, it is said that Alexander Graham Bell had a certain intuition of the transmission of sound by observing the waves of water on a river.

⁹ To detect waves and make them perceptible, measure their frequency using a rotating mirror stroboscope, check Maxwell's propagation equations...

To broadcast a program, the voice is transformed into an electrical signal by the microphone. This signal oscillates at the same rate as the voice; they have the same frequency (expressed in hertz). The antenna emits a modulated electromagnetic wave, which propagates to the receiving antenna of the radio set.



Figure 6: Radio transmission diagram

Also called radio frequency (RF), radio or hertzian waves range in frequency from ten kilohertz (KHz) to three hundred gigahertz (GHz)¹⁰. They travel longer or shorter distances. The lower the frequency of the waves, the further they propagate and vice versa.

Bluetooth (2.4 GHz), for example, has a range of a few meters and FM radios (between 87.5 and 108 MHz) a range of a few tens of kilometres.

In France, the first regular radio broadcasts began on Christmas Eve 1921 with Radio Tour Eiffel¹¹, picked up by a handful of "wireless operators" on a wavelength of 2,650 meters. Unlike American stations which broadcast on short and medium waves, the first French stations chose to broadcast on long waves, both for technical and commercial reasons. On the one hand, they are better captured; on the other hand, they cannot be picked up by American receivers (protection of the nascent radioelectric industry in France).

One hundred years later, radio frequencies are present everywhere: used by mobile phones, tablets, navigation assistants (GPS), connected objects, microwave ovens, lasers, etc.

According to INSEE, more than 95% of the population aged over 15 has a mobile phone.

And more than 40 million people listen to the radio every day¹².

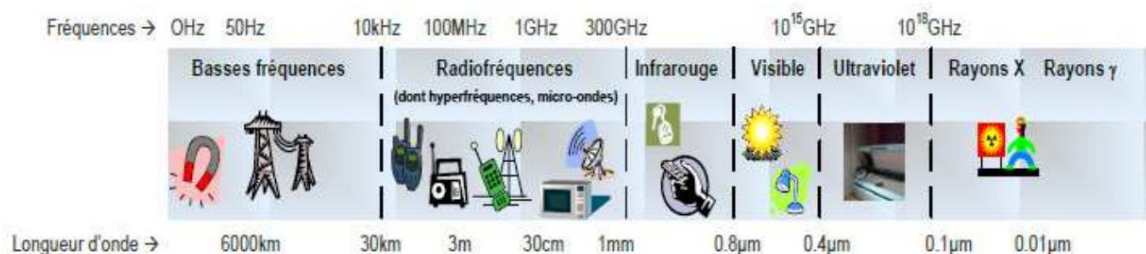


Figure 7: The spectrum of electromagnetic waves

¹⁰ As defined by the International Telecommunication Union (ITU): <https://www.itu.int>

¹¹ From December 24, 1921 to June 6, 1940.

¹² Insee, *ICT household survey between 2009 and 2021*.

Electromagnetic waves are characterized by a set of parameters: frequency, wavelength, electric field intensity, magnetic field intensity, propagation speed, etc. “Like all electromagnetic waves, radio frequencies can interact with living matter depending on their frequency and intensity. Yann Percherancier specifies¹⁴ : “They can propagate in matter: therefore, in our organism. While human beings have been exposed to artificial electromagnetic radiation for a long time, especially by radio, its biological effects are highly debated due to conflicting results.

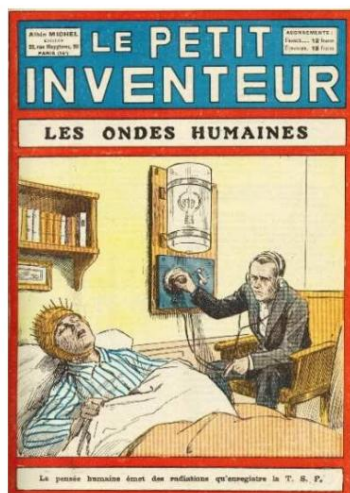


Illustration 8: Human waves (The Little Inventor, 1928)

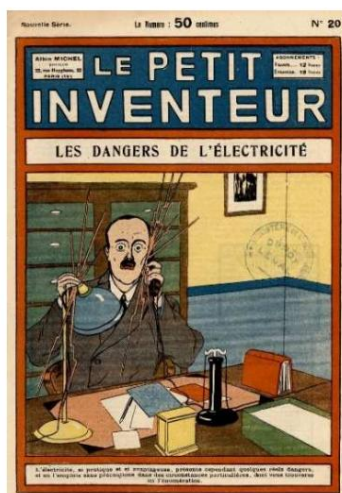


Illustration 9: The dangers of electricity (The Little Inventor, 1928)

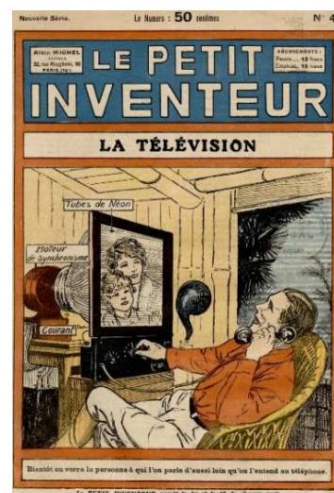


Illustration 10: Television (The Little Inventor, 1929)

Bio-electromagnetism

Bioelectromagnetism is the field of study of the mechanisms of interaction of radio frequency electromagnetic fields with living matter as well as the biological effects induced by exposure to radio frequencies. Despite the intensity of research efforts, our knowledge of bio-electromagnetics has not been able to keep up *with the rapid evolution of technologies*.

In fact, the extrapolation of knowledge from previous generations of mobile telephony to new signals remains difficult :

- On the one hand, the signals have distinct characteristics (e.g. different depths of body penetration, absorption patterns, amplitude modulation) ;
- On the other hand, the concept of extrapolation is not unanimous.

New communication technologies

Today, new wireless communication technologies have taken on crucial importance in our contemporary society. Practices are developing and diversifying. In 2021, 86% of

¹³ Used in physics, the notion of field reflects the influence that an object can exert on its environment from a distance.

¹⁴ Yann Percherancier, *5G signals and multiple exposures*, pp. 17-19.

people residing in France have used the Internet in the last three months, compared to only 65% in 2009¹⁵.

This growth is accompanied by a permanent evolution of the radio signals used to convey the information transmitted (voice, data, etc.). The uses of these technologies, as well as the characteristics of the signals (frequency band, modulations, power levels, etc.) coexist with different generations of previous systems.

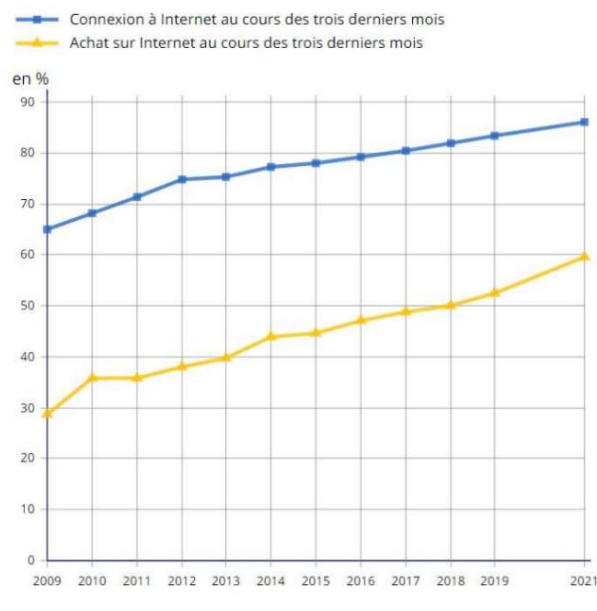


Illustration 11: Percentage of people (over 15) who have connected to the Internet or made an online purchase in the last three months (Source: Insee, 15 Feb. 2022)

As Rémy Pedoux points out, the intensive use of new communicating objects and access to ever-increasing online services leads to "the saturation of existing frequency ranges and requires the use of higher carrier frequencies, including 5G technology. and millimeter waves"¹⁶.

The 5th generation

Initiated in Europe since 2020, the commercial deployment of 5G technology (for "5th generation") aims to provide digital services and applications, both for individuals and businesses in multiple areas (eg gaming network, virtual reality, audio and video streaming, telemedicine). It carries a promise of a digitized society where all everyday objects will be able to communicate with each other: smart cities and transport, industrial automation, online education... Depending on the development and adherence to these new uses, they are likely to significantly modify exposures of the population; they therefore require research and expertise to assess the potentially associated health effects.

¹⁵ Insee, *ICT household survey between 2009 and 2021*.

¹⁶ Rémy Pedoux, *DNA damage and millimeter waves*, pp. 35-37.

• 5G versus 4G

One of the purposes of deploying the 5G mobile network is to increase speeds (up to ten times faster than those of 4G) to promote data exchange without clogging existing networks. Two new frequency bands have thus been assigned to 5G: 3.5 and 26 gigahertz (GHz) which will coexist with previous generations of mobile telephony.

Protocols have been defined. Commercial deployment in the 3.5 GHz band began in November 2020, while some mobile operators are already carrying out pilot experiments in the 26 GHz band in several cities¹⁷ to test the new infrastructures under development.

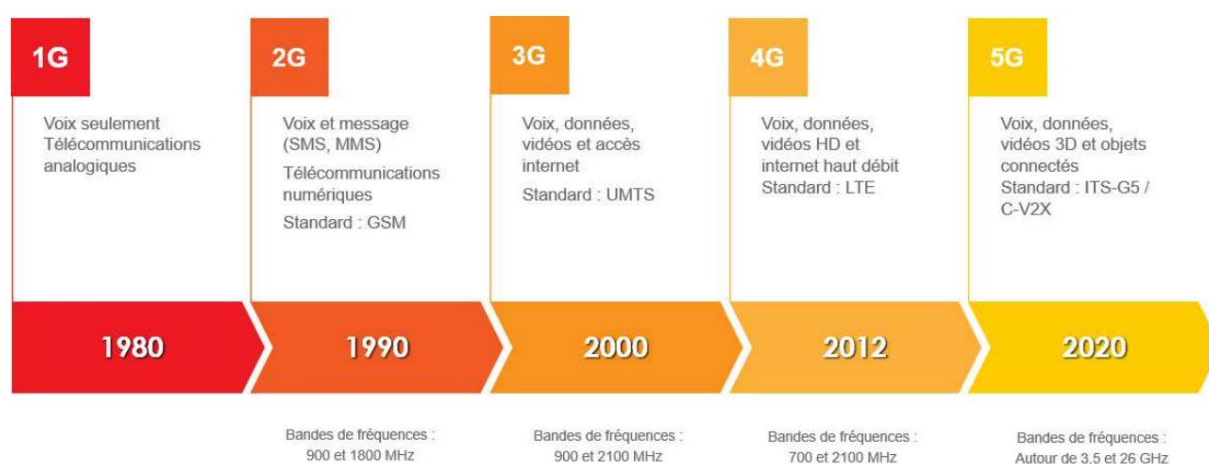


Figure 12: Evolution from 1G to 5G in France

• New network infrastructures

With regard to 5G, the use of new higher frequencies also implies a multiplication of antennas, i.e. access points to the telecommunications network (eg base stations). Indeed, the low frequency bands are those which have the greatest wavelength. On the other hand, high frequency bands such as 3.5 and 26 GHz deliver better throughput, but they have a more limited signal range: respectively, approximately 400 meters and 150 meters in urban areas¹⁸. The visible increase in the number of transmitters may lead to growing concern for the potential effects of multiple RF exposure on human health.

Two of the projects presented in this new issue of *Cahiers de la Recherche* thus focus on the effects resulting from multiple (or combined) exposure to 5G signals : • EXPOAUTO which aims to characterize, according to Gabriella Tognola¹⁹, "the cumulative exposure of passengers and pedestrians to electromagnetic fields resulting from the technologies » present in the automotive ecosystem (connected cars) ;

¹⁷ Dashboard of 5G experiments in France: <https://www.arcep.fr/cartes-et-donnees/nos-publications/figures/experimentations-5g-en-france/tableau-de-bord-des-experimentations-5g-en-france.html>

¹⁸ For comparison, the 700 MHz frequency band has a range of 2 km in urban areas.

¹⁹ Gabriella Tognola, *Connected cars*, pp. 15-17.

- **5G-SAMU** which assesses on the one hand, the potential effects induced by 5G signals at 3.5 GHz "on cellular reactions to stress, such as the adaptive response and autophagy"²⁰ (Yann Percherancier) and on the other hand, the potential effects of combined exposure with GSM (2G) and continuous wave (CW) fields. It complements the project led by Muriel Priault on the adaptive response to radio frequencies²¹ .

A risk of overheating

The ability of radiofrequencies to cause tissue heating is well characterized, exposure limit values have thus been defined in order to protect populations from possible thermal effects. The recommendation of the Council of the European Union of June 12, 1999 is based on the limit values defined by the International Commission on Non-Ionizing Radiation Protection (ICNIRP): 0.08 W/kg for the whole body, 2 W/ kg for head and trunk. Regularly reassessed, these values have not been called into question by the latest SCENIHR²² reports on emerging and new health risks, nor by ICNIRP itself recently, in 2020. However, ANSES is closely monitoring the evolution of these standards; it analyzes and comments on the draft texts submitted for public consultation.

- **Safety margin**

In establishing its limit values, ICNIRP takes a margin of safety. Studies on animals, human cells and numerical models have shown that a thermal effect²³ can occur when the specific absorption rate (SAR) exceeds the value of 4W/kg for the whole body and 100 W/kg for certain most exposed parts of the body such as the head and the trunk. A coefficient of 50 was therefore applied to warn the population of any possible thermal effect.

However, wonder René de Sèze and Brahim Selmaoui, "laboratory experiments have shown changes in homeostasis (eg temperature) in juvenile rats exposed to low intensity RF. ²⁴ Hence the objective of the MOTHER project "to assess in real time on living matter the potential effects of exposure to RF fields (LTE, 5G)".

Possible biological effects

For twenty years, studies have evoked other possible effects: non-thermal. Particular attention has been paid to the potential effects of radio frequencies on living matter, ie on biological effects. However, the results obtained are often contradictory and the lack of reproducibility²⁵ does not allow robust conclusions to be drawn.

²⁰ Yann Percherancier, *5G signals and multiple exposures*, pp. 17-19.

²¹ Muriel Priault, *The adaptive response to radio frequencies*, pp. 38-39.

²² Independent scientific committee set up in 2004 by the European Commission to advise it on the risks emerging and new sanitary facilities.

²³ The value of 4W/kg corresponds to an increase of 1°C in the human body.

²⁴ René de Sèze and Brahim Selmaoui, *The potential effects of radiofrequencies on thermoreceptors*, pp. 20-21

²⁵ The reproducibility criterion is one of the conditions which makes it possible to avoid random effects or errors of judgement. According to Karl Popper, conclusions can only be drawn from a well-characterized event, which has occurred several times and caused by different people.

Concerning the exposure of workers to the risks due to physical agents, the directive 2013/35/EU of the European Parliament and of the Council of June 26, 2013 covers “all known direct and indirect biophysical effects produced by electromagnetic fields”²⁶ :

- Thermal effects such as tissue heating ;
- Non-thermal effects such as stimulation of muscles, nerves or sensory organs ;
- Indirect effects such as interference with electronic medical equipment and devices, contact currents, etc.

However, in the current state of scientific knowledge, the directive only deals with potential short-term effects; it does not address the potential long-term effects of RF exposure, or even multiple exposure. However, due to the omnipresence of radiofrequencies, even a small health risk could have a major impact on public health.

Possible carcinogens

Started in 2000, the Interphone²⁷ study remains to this day the largest case-control study conducted on the use of mobile phones and the risk of brain cancer in thirteen countries²⁸ using a common protocol. It brought together 2,708 cases of glioma²⁹, 2,409 cases of meningioma³⁰, 1,121 cases of acoustic neuroma³¹ (or schwannoma), 109 tumors of the parotid gland³² and 7,658 controls belonging to the same age group (between 30 and 59 years old). . According to Dr. Christopher Wild³³, the data collected did not “demonstrate an increased risk of brain cancer”³⁴. But they also did not allow us to conclude that there is no risk. Among the most debated issues: cell phone use and the risk of glioma.

From May 24 to 31, 2011, international experts gathered in Lyon³⁵ under the aegis of the International Center for Research on Cancer (Circ). After analyzing hundreds of scientific papers and reviewing all of the associated data, they considered the evidence of carcinogenicity to be “*limited*”³⁶ in wireless phone users for glioma and acoustic neuroma, and “*insufficient*”³⁷ for be conclusive for other types of cancers . Thus, they classified the

²⁶ Art. 1.2 (Object and scope) and Art. 2 (Definitions).

²⁷ Website: <https://interphone.iarc.fr/>

²⁸ Germany, Australia, Canada, Denmark, Finland, France, Israel, Italy, Japan, Norway, New Zealand, United Kingdom and Sweden.

²⁹ Glioma is the most common form of brain tumour. This cancer begins in the glial cells, which surround and support nerve cells.

³⁰ A slow-growing type of tumor that forms in the meninges (thin membranes that surround and protect the brain and spinal cord).

³¹ Almost always benign tumor of the peripheral nervous system.

³² The parotid gland is the largest of the salivary glands.

³³ Director of IARC, from 2009 to 2018.

³⁴ IARC, *Publication of the Interphone study on the use of mobile phones and the risk of brain cancer*, Press Release No 200, 17 May 2010.

³⁵ From May 24 to 31, 2011.

³⁶ A positive association has been established between exposure to the agent under consideration and the occurrence of cancers, and the working group considers that a causal interpretation of this association is credible, but it has not been possible to exclude with sufficient certainty that chance, bias or confounding factors may have played a role.

³⁷ The available studies are not of sufficient quality, agreement or statistical power to conclude whether or not there is a causal relationship between exposure and cancer, or although no data on cancer in humans are available.

³⁸ IARC, *IARC classifies radiofrequency electromagnetic fields as “possibly carcinogenic to man”*, Press Release No 208, 31 May 2011.

radiofrequencies as “possibly carcinogenic to humans” (group 2B). According to Dr Jonathan Samet³⁹, chairman of this working group: "This classification means that there could be a risk, and that we must therefore closely monitor the possible link between mobile phones and the risk of cancer".

Among the confounding factors that prevent the establishment of a causal relationship, Joachim Schüz lists the biases and errors that limit the strength of the conclusions⁴⁰. Additionally, the majority of cases and controls in the Interphone study were not heavy mobile phone users by current practice. Today, mobile phone use has become much more widespread. What about children and teenagers? Do they have an increased risk of brain tumour?

In addition to the international Mobi-Kids⁴¹ study, the objective of the project presented by Monica Guxens (EXPO-ENFANTS) is to identify the practices and analyze the social determinants of the real exposure of children (at different ages) to radio frequencies⁴² of mobile phones, connected objects and new technologies.

A constant scientific watch

Faced with the sustained pace of publications in this field, ANSES maintains a permanent scientific watch on the subject. Since its last global expert report devoted to the health effects of exposure to radiofrequencies (2013), it has produced several specific expert reports, in particular on :

- The effects of radiofrequencies on health (2016) ;
- Hypersensitivity to electromagnetic fields (2018) ;
- Exposure to high SAR phones (2019) ;
- Exposure to electromagnetic fields linked to the deployment of 5G (2020-2022).

A research program

At the same time, ANSES has created a “Radiofrequencies and health” research program, endowed with two million euros per year. Led by a dedicated scientific council, it has launched a call for specific research projects since 2013, following the same schedule as that of the national research program “Environment Health Work” (PNR EST).

The increasing use of mobile phones raises many questions. How to assess the potential biological effects induced by electromagnetic fields? How to decipher these subtle interactions between living matter and low-level radio frequencies ?

³⁹ University of Southern California, USA.

⁴⁰ Joachim Schüz, *The biases (factors) of confounding*, pp. 22-24.

⁴¹ Mobi-Kids is an international epidemiological survey involving 900 brain tumor patients and 1,900 controls from 14 countries. Brigitte Lacour, Thomas Remen, Martine Hours, Elisabeth Cardis. Brain tumors and mobile telephony in young people. *The Research Papers. Health, Environment, Work*, ANSES, 2016, Views on 10 years of research, the PNR EST from 2006 to 2015, pp.33-34. [janses-01772417](#) ⁴² Monica Guxens, *Uses and exposure of children to new technologies*, pp. 24-26

To understand electromagnetic hypersensitivity (EHS), Anne Pereira de Vasconcelos offers “a unique approach” in an animal model which opens up new perspectives⁴³. Due to the proximity of mobile phones to the head, explains Bruno Bontempi, “it is the central nervous system (CNS) that is the subject of the greatest questions”. During periods of heightened sensitivity such as the prenatal period, “some studies conducted in mammals show that genes and environment act in concert”⁴⁴. His WIFIDEV project thus aims “to assess the effect of these exposures on the development of embryos as well as on the development of the brain and its functioning in adulthood”⁴⁵.



Figure 13: RF exposure and children's health (ANSES, June 2016)



Figure 14: Electromagnetic hypersensitivity or idiopathic environmental intolerance attributed to electromagnetic fields (ANSES, March 2018)



Figure 15: Exposure to electromagnetic fields linked to the deployment of “5G” technology (ANSES, February 2022)

Delia Arnaud-Cormos is exploring a recent brain imaging technique, neuro-imaging, to observe brain activity *in vivo* (in real time) and functional connectivity in mice exposed to radiofrequencies” in the least invasive way possible⁴⁵. Similarly, the work presented here by Michel Mallat is based on *in vivo* or *in vitro* animal models ; which makes it possible to better understand the biological effects of RF and their possible health impacts. “They support the hypothesis of an increase in the sensitivity of brain cells to GSM or 4G LTE signals during neuroinflammatory reactions. »⁴⁶

43 Anne Pereira de Vasconcelos, *The rat as an animal model for the study of electromagnetic hypersensitivity*, pp. 26-28.

44 Bruno Bontempi, *Prenatal exposure to WiFi*, pp. 33-35.

45 Delia Arnaud-Cormos, *New approach to measuring cerebral activity under RF*, pp. 29-30.

46 Michel Mallat, *Variation of the intracerebral effects of radiofrequencies according to the state of health*, pp. 31-33.

connected cars

Cumulative exposure induced by radiofrequency electromagnetic fields induced in humans by new technologies associated with automotive services and connected objects

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Partner teams: Joe Wiart, Institut Mines Telecom, Telecom Paris Tech, 2M Chair, Paris – Joseph Wout, IMEC Waves Research Group, Gent, Belgium

Research project (ongoing since Dec. 2020 - Duration: 40 months) - Funding: €239,928 - Contact: gabriella.tognola@ieiit.cnr.it

Keywords: technology, automobile, information and communication technologies, exposure, radio frequency, internet, communications, wave absorption, dosimetry, dosimeter, electromagnetic field, electromagnetic radiation

As of today, 98% of new cars sold worldwide are connected to

Internet and equipped with information and communication services⁴⁷. In France, 12.8 million cars are already connected⁴⁸ for the purposes of navigation assistance (e.g. traffic information, driving assistance, danger zone notification for the driver) and infotainment services (streaming music, video on demand for car passengers) so that they give a good overview of the "internet of things" (IoT in English).

⁴⁷ *Connected cars, facts and figures*, Statista Research Department, 2021 : https://fr.statista.com/themes/3695/les-voitures-connectees/#dossierContents_outerWrapper

⁴⁸ Projection of the number of connected cars in circulation in France from 2017 to 2022, Statista Research Department, 2022 : <https://fr.statista.com/statistiques/669112/projection-nom-voitures-connectees-circulation-france/>

The automotive ecosystem

In a recent car, connectivity is based on LTE49 and LTE Advanced (4G) network technologies. It shapes the driver experience by providing at the level the

more basic, information on driving assistance (e.g. location, traffic, safety) and also generates growing needs: hence the proliferation of sensors on vehicles and the presence of screens (or even multi-screens) inside the cabin.

To promote the exchange of information and improve two the communication, technologies are available : •

ITS-G5 (derived from Wi-Fi) which uses the 5.9 GHz frequency band ; • C-V2X, which uses the cellular networks of mobile telephone operators and must eventually integrate 5G.

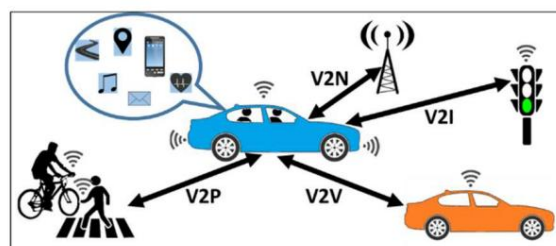


Figure 16: The automotive ecosystem (Credits: Gabriella Tognola)

But, these two technologies are not interoperable, that is to say that a car equipped with one technology cannot communicate with a car equipped with the other technology. In this context of digital transition, the European Commission responsible for the deployment of "Intelligent Transport Systems" (ITS) issued a delegated regulation in March 2019 which gives the advantage to ITS-G5 while leaving the door open to other technologies that may be deployed in the future.

⁴⁹ From English " Long Term Evolution" (standard in telecommunications defined by the 3GPP).

In addition, the connected car ecosystem involves, in addition to car manufacturers, a large number of players such as equipment manufacturers. It also supposes adapting the road infrastructures (eg road sensors, communicating panels, communication networks) so that the question of the exposure of the population is far from being trivial.

Exposure scenarios

The automotive ecosystem forms a complex and dynamic environment, due to the multitude and variety of factors that can influence exposure (e.g. distance from sources, type and number of technologies embedded in the car, road infrastructure, the number of connected cars nearby, the context of use⁵⁰, characteristics of people, etc.). Building a deterministic model of exposure variables likely to influence exposure have been identified and that the cause-effect relationships of cause-effect

between these variables have been clarified and characterized; which is practically impossible.

To anticipate what will be the exposure of the population in this new ecosystem, we are considering innovative probabilistic (statistical) approaches, based on previous studies already funded by the PNR EST: **Mobi-Expo⁵¹**, **CREST⁵²**, **AMPERE⁵³**, **EXPO-**

⁵⁰ Ex. during short trips versus long trips, during daily commutes, during leisure trips...

⁵¹ **Mobi-Expo**, *Characterization of the conditions of use of mobile phones and exposure to radiofrequencies in a multicentre epidemiological study*, project led by Martine Vrijheid (2011-RF-216)

⁵² **CREST**, *Characterization of exposure to radio frequencies (RF) induced by new uses and new technologies of mobile communication systems*, project led by Elisabeth Cardis (2013-RF-22)

CHILD... without forgetting possible synergies with European projects such as **GERoNiMO54** and **CONCORDA55**.

The research project: **EXPOAUTO**

The automotive ecosystem is at the heart of the EXPOAUTO project, the main objective of which is to characterize the cumulative exposure of passengers and pedestrians (adults, children, newborns, pregnant women, etc.) to electromagnetic fields resulting from the technologies present in the automotive ecosystem, including 5G.

Methodology

The methodology implemented is based on four phases: 1. *Identify the technologies, protocols and modes of use of the different*

IoT devices in connected cars, road infrastructure and people

2. *Measure electromagnetic fields emitted by connected cars under real⁵⁶ and experimental conditions*

pedestrians, in different organs and tissues (including, the eyes)

4. *Determine the cumulative exposure of connected car users and*

pedestrians (based on the results obtained in phases 2 and 3) with advanced statistical methods (e.g. algorithms of

⁵³ **AMPERE**, *Characterization of residential exposure to RF waves*, project led by Joe Wiart (2016-RF-4)

⁵⁴ **Generalized EMF Research using Novel Methods**, <https://www.isglobal.org/en/-/geronimo-generalized-emf-research-using-novel-methods-an-integrated-approach-from-research-to-risk-assessment-and-support-to-risk-management> ⁵⁵ **Connected Corridor for Driving Automation**, <https://ertico.com/concorda/> as part of the European H2020 program.

⁵⁶ On the road in Belgium, France and Italy.

" *Machine Learning* ", taking into account random or stochastic effects) capable of modeling the complexity of reality.

Preliminary results

The activities carried out so far have focused on the technical and electromagnetic characterization of the main technologies (eg Bluetooth, WiFi, 4G/5G) used in the connected car and automotive radars.

These characteristics derive both from the examination of technical standards and from experimental measurements carried out in the laboratory and on the road with a real car.

Regarding the RF exposure dose for vehicle passengers and pedestrians near the connected car, numerical simulations are performed using realistic human phantoms to assess whole-body and local exposure in different tissues and organs (eg skin, head, eyes and genital area).

Publications:

Tognola G, Bonato M, Benini M, Aerts S, Gallucci S, Chiaramello E, Fiocchi S, Parazzini M, Masini BM, Joseph W, Wiart J, Ravazzani P, "Survey of Exposure to RF Electromagnetic Fields in the Connected Car," *IEEE Access*, 2022, 10, p. 47764-47781, 2022, doi: 10.1109/ACCESS.2022.3170035.

Bonato M, Tognola G, Benini M, Gallucci S, Chiaramello E, Fiocchi S, Parazzini M, "Assessment of SAR in Road-Users from 5G-V2X Vehicular Connectivity Based on Computational Simulations," *Sensors*, 2022, 22, p. 6564. doi: 10.3390/s22176564

Benini M, Parazzini M, Bonato M, Gallucci S, Chiaramello E, Fiocchi S, Tognola G, "Road user RF exposure from ITS-5.9 GHz vehicular connectivity,"

Sensors, 2022, doi: 10.3390/s22186986

5G signals and multiple exposures

5G signals and multiple exposures: looking for cellular and molecular effects

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Research project (ongoing since January 2020) – Funding: €242,299 – Contact :

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Key words : multiple exposure, exposure, radio frequency, cellular stress, cell, molecule, skin cells, neurons, telecommunication, technology, communications, public health

For twenty years, radio frequencies have been present everywhere: widely used in the field of telecommunications (mobile phones, tablets, connected objects, etc.). To avoid the risk of network saturation and make data sharing more fluid, the fifth generation (5G) of wireless networks must gradually replace the fourth (4G)⁵⁷ by offering higher speeds and shorter latency times.

There were thus more than five billion mobile users in the world in

January 2020: i.e. 67% of the total population⁵⁸

Uncertainties

Like all electromagnetic waves, radio frequencies (RF) can interact with living matter depending on their frequency and intensity. They can propagate in matter: therefore, in our organism. Among

⁵⁷ LTE advanced (long-term evolution)

⁵⁸ From January 2019 to January 2020, the number of mobile users increased by 2.4%. This growth was faster than that of the world population, which only grew by 1.1% over the same period.

(Source: *We are Social Digital 2020* report)

the effects produced, a distinction is made between thermal effects⁵⁹ and “non-thermal” effects⁶⁰ which, to date, are the subject of debate. Indeed, RF have distinct characteristics (eg different penetration depths in the body, absorption patterns, amplitude modulation). While the ability of RF to induce tissue heating⁶¹ is well characterized, uncertainties remain about the potential biological effects that could result from exposure to low-intensity electromagnetic fields.

Amplitude modulation

Although the majority of recent studies have reported no effect specific to amplitude modulation⁶², some studies (including ours) indicate possible specific effects of amplitude modulated RF signals on the electrical activity of neurons. However, no plausible hypothesis can explain the underlying mechanisms of these so-called “non-thermal” effects⁶³. In the absence of reliable and reproducible effects, it is therefore difficult to draw conclusions.

To our knowledge, no study has yet evaluated the effect of 5G signals (emitted alone or in combination with other signals) on living matter. Assessing whether or not new RF technologies induce a cellular stress response *in vitro* or impact the electrical activity of neurons under well-controlled exposure conditions is an essential step for safe deployment and risk assessment of all effects. health potentials of 5G signals.

⁵⁹ Physically validated.

⁶⁰ These “non-thermal” effects refer to effects that are not caused by elevation of tissue temperature.

⁶¹ Dielectric relaxation.

⁶² Used to transfer information.

⁶³ That is, which are not caused by the rise in temperature of living tissues.

The research project: 5G-SAMU

In a previous study⁶⁴, we identified a potential differential response induced by GSM (2G) fields and pulse modulated CW waves. At 17-28 days, neuronal cultures⁶⁵ were subjected *in vitro* to fifteen-minute RF exposures, at SARs ranging from 0.01 to 9.2 W/kg. GSM and CW signals resulted in a sharp decrease neuronal differentiation during exposure. This effect became more pronounced for higher SAR levels and continued beyond the end of exposure. Note: at an average SAR level, the amplitude of the effect was greater with the GSM signal than with the CW.

Our studies thus provide unique evidence for decreased electrical activity of cortical neuronal cultures during RF exposure and suggest that part of the mechanism is non-thermal.

These results are similar to those of a American research group and therefore require an evaluation of the effects of 5G modulation at 3.5 GHz on the electrical activity of neurons.

During the last twenty years, the possibility that RF exposure induces cellular stress responses in other cell types has been evaluated taking into account different biochemical phenomena (e.g. DNA integrity, repair capacity, apoptosis⁶⁶, protein expression). The effects observed were weak, often close to the detection limit. In 2013, the IARC working group therefore concluded that there was little evidence that RF fields induce apoptosis in human cells *in vitro*.

But since then, the number of studies relating to the apoptotic effects of RF in lines

⁶⁴ MOTUS, *RF Signal Modulation and effects on the brain: in vivo and in vitro approach*, study funded by the PNR EST (2015-RF-19) ⁶⁵ From embryonic cerebral cortices of rats.

⁶⁶ Programmed cell death.

cellular and primary cells increased significantly.

Goals

The potential effects of RF signals on cellular responses to stress, such as the adaptive response and autophagy, are of growing interest. Currently, we are evaluating the effect of UMTS (3G) fields at 1.95 GHz on these two cellular mechanisms⁶⁷. We propose to complete this study in the context of exposure to 5G signals.

The effects of 5G signals will be systematically compared to CW signals at 3.5 and 1.8 GHz. Finally, we plan to study the effect of the combined exposure of 5G at 3.5 GHz and GSM at 1.8 GHz.

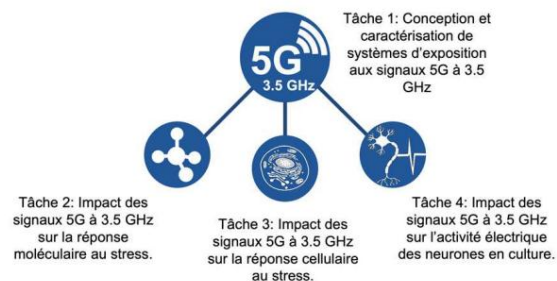


Figure 17: The 5G-SAMU research project (Credits: Yann Percherancier)

Our objective here is to determine whether 5G RF fields at 3.5 GHz (at various levels of SAR up to 4W/kg) are able to :

- Decrease the activity neuronal electrical, as we have already observed for the 2G signal at 1.8 GHz
- Induce a cellular and molecular response to stress in cells targets of 5G signals such as fibroblasts and keratinocytes of the skin.

The RAS/MAP68 kinase pathway, heat shock protein activation, induction of mitochondrial stress, endoplasmic reticulum stress and apoptosis will be measured after exposure to 5G signals at 3.5 GHz.

⁶⁷ ADAPT, *Adaptive response to radiofrequency fields: is autophagy the key ?*, study funded by the PNR EST (2017-RF-12)

⁶⁸ From the English " *Retrovirus Associated Sequences* " and " *Mitogen-activated protein* "

The potential effects of radio frequencies on thermoreceptors

Numerical modeling of the interaction of RF fields on thermal receivers: mechanisms and experiments long live and Vitro

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Research project (ongoing since Nov. 2020 - Duration: 40 months) - Funding: €199,935 - Contact: brahim.selmaoui@ineris.fr

Keywords: radiofrequency, interaction, modeling, thermoregulation, body temperature, receptor, antagonist, mechanism of action, animal experimentation, in vivo, in vitro, model, molecule, dosimetry, mouse, information and communication technologies

To date, the only known and validated effects of radiofrequency (RF) on living matter are thermal effects such as tissue heating. Because of associated risks, recommendations and standards have been defined in order to ensure the protection of the general population (basic restrictions). Thus, the limit values for exposure of people to electromagnetic fields imposed by the regulations correspond to the specific absorption rate (SAR), which is expressed in watts per kilogram (W/kg): 0.08 W/kg (body whole) and 2W/kg (for the head or trunk)⁶⁹.

⁶⁹ Decree No 2002-775 of May 3, 2002 which transposes into French law European recommendation 1999/519/EC of July 12, 1999 based on the ICNIRP guide for establishing exposure limits (1998).

However, laboratory experiments have shown changes in homeostasis (e.g. temperature) in juvenile rats exposed to low intensity RF⁷⁰

Thermoregulation

Exposed to hot or cold, the body implements regulatory mechanisms that allow it to maintain a desired temperature. These mechanisms are based on a constant balance (homeostasis) between heat intake and heat loss (eg food intake, locomotor activity, sleep).

After exposing rats⁷¹ for five weeks (23 hours a day, 7 days a week) to low intensity waves⁷², it was observed that they adopted a strategy of avoiding the lowest temperatures⁷³

This reaction would come from an increased sensitivity to cold due to a direct effect of RF on thermoreceptors possessing a TRPM-8 protein, itself sensitive to cold. Faced with this hypothesis, the question of the potential effects of RF on living matter at the cellular and molecular levels arises in particular on the proteins involved in the response to cellular stress such as other channels TRP⁷⁴

⁷⁰ Amandine Pelletier, Jean-Pierre Libert, *Cumulative effects of ONIEs: co-exposure to ONIEs and thermal stress*, Cairn.info : <https://doi.org/10.3917/re1.103.0023> Publi (2013). "Effects of chronic exposure to radiofrequency electromagnetic fields on energy balance in developing rats." *Environmental Science and Pollution Research* 20(5): 2735 - 2746 ⁷¹ Three weeks old.

⁷² Of the type emitted by relay antennas (900 MHz, 1 V/m, 0.3 W/kg).

⁷³ The animals were free to move around in three enclosures each regulated at different temperatures (24, 28 and 31°C).

⁷⁴ From the English " *Transient Receptor Potential* ".

The BRET technique

Over the past twenty years, approaches based on resonance energy transfer (RET) have offered new possibilities for monitoring in real time and on living cells, the interactions between proteins or their conformational changes. In order to be able to expose living cells to RF fields, this technique required the development of an experimental device using BRET (bioluminescence) probes, based on temperature-sensitive TRP channels and on optical fibers connected to a spectrometer. . This promising technique is increasingly used for the study of protein activity in living matter⁷⁵ .

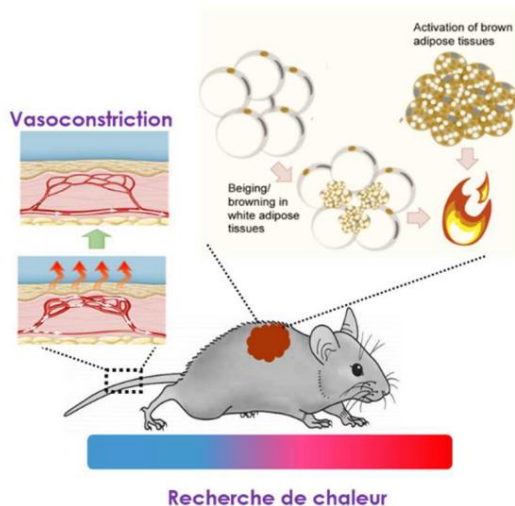


Illustration 18: Thermal regulation, in response to cold
(Author: Thi Cuc Mai)

The research project: MOTHERR

The objective of this study is to evaluate in real time on living matter (fibroblasts

⁷⁵ RF-BioCell, *Real-time study of the global cellular effects of radiofrequency fields*, project led by Yann Percherancier (2013-RF-195) - Yann Percherancier.

Thesis for obtaining the Habilitation to Direct Research Study of the cellular and molecular effects of electromagnetic fields. Life Sciences [q bio]. University of Bordeaux, 2017.
jtel-02525164j

and cell lines) the potential effects of exposure to RF fields (LTE, 5G)⁷⁶ by monitoring the activity of TRP ion channels using the BRET technique.

Methodology

In parallel, we will conduct *in vivo* pharmacological experiments with different active compounds (drugs) to verify the specificity of the observed effects and their correlation with *in vitro* experiments.

In addition, a numerical model (molecular dynamics) will make it possible to describe the mechanisms of interaction and to check whether the observed effects can be explained by “classical” models of interaction. The study of the effects of RF on the various thermal receptors will also be sought, depending on ambient temperatures and cold (eg possible interaction of agonists/antagonists).

Preliminary results

- TRP probes have been designed and their response as a function of temperature has been characterized. The first results with RF exposure showed no change.
- Models of TRP receptor channels have been developed to study the interaction of radio frequencies with their configuration. • The use of antagonists showed different effects on thermal kinetics between exposed and control animals. • An effect on the stimulating hormone thyroid TSH was observed, and hormone concentrations thyroid T3 and T4 are studied in more detail.

⁷⁶ From 4 mW/kg to 4W/kg.

The biases (factors) of confounding

Cell phones and glioma risk: the effect of various errors in the risk estimate of the multinational Interphone case-control study

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Keywords: mobile phone, risk of glioma, measurement error, evaluation, simulation

The International Center for Research on Cancer (IARC, Lyon) classified radiofrequency electromagnetic fields (RF-EMF) in 2011 as possibly carcinogenic (Group 2B)⁷⁷. Although to date the evidence from the literature has been considered limited, in particular because of some divergent results, some case-control studies on the subject have reported positive associations. The results of the largest case-control study conducted (INTERPHONE⁷⁸) involving 13 different populations, between mobile glioma – the most common form of brain tumor – with an increase in 40% risk among the top 10% of mobile phone users. This study also showed a significant decrease

of glioma risk among low or moderate users which was considered biologically unlikely and interpreted as clear evidence of the presence of bias and confounding factors within the study. It is therefore essential to identify

the types of biases or measurement errors that could drive a similar hazard function in order to obtain a valid interpretation of the results of this study.

Potential bias

The main results of the study

INTERPHONE suggest a "J"-shaped exposure-risk relationship between mobile phone use and the risk of glioma and in particular : • Increased risk (*odds ratio*,

OR > 1) glioma among the most “heavy users” of mobile phones⁷⁹; • Significant reduction in risk

(OR < 1) of glioma among light or moderate users⁸⁰

However, a protective effect of mobile phone use on glioma risk among light or moderate users – compared to non-regular users – is very unlikely from a biological point of view and would therefore reflect the presence of biases and exposure measurement errors in the INTERPHONE study.

The participants (glioma cases and controls⁸¹) of the INTERPHONE study were questioned using a questionnaire on their past use of the mobile telephone. Self-reporting of mobile phone use may be biased. Among the main biases identified and discussed are :

⁷⁷ International Agency for Research on Cancer (IARC). Non-ionizing radiation. Part 2, Radiofrequency electromagnetic fields. IARC monographs on the evaluation of carcinogenic risks to humans. Flight. 102, Lyon, 2013 2 International Journal of Epidemiology, Volume 39, Issue 3, June 2010, Pages 675–694, <https://doi.org/10.1093/ije/dyq079> - Website : <https://interphone.iarc.fr/>

⁷⁹ OR=1.40; 95% CI (confidence interval), 1.03–1.89.

⁸⁰ OR = 0.81; 95% CI (confidence interval), 0.70–0.94.

⁸¹ Witnesses drawn by lot from the electoral lists.

- **Participation (or selection) bias:** differential participation bias among controls, where reported mobile phone use was greater among control participants than non-participants in the study leading to an over-representation of users ; thus creating a false association with mobile phone use.

- **Recall (or memorization) bias of mobile phone exposure/use :** An underestimation of

the postponed use of the mobile phone among the low users and, conversely, an over-estimation of the use by the most important users were observed. In addition, implausible (exaggerated) values of self-reported use of

mobile phone were more frequent among cases than controls, which could *ultimately* lead to a fictitious positive association (which could somehow suggest the origin of their disease).

The research project: INTER-CAL

The main objective of this study is to create a scientifically coherent model of the various biases and uncertainties present in the INTERPHONE case-control study, in order to determine whether the risk estimates reported in this study could be compatible with the hypothesis of no association between mobile phone use and glioma risk; once uncertainties and biases have been taken into account.

Methodology

We relied on Monte-Carlo type simulation analyzes based on

a “logistic regression”⁸² model to estimate the risk of glioma according to categories (deciles⁸³) of mobile phone use. Based on available data from validation studies of the case-control study

INTERPHONE, several scenarios of biases and uncertainties have been defined and examined in comparing self-reported data by participants (which may be biased and assumed to be subject to error) to those provided by mobile operators (assumed “true”).



Figure 19: Interphone website, <https://interphone.iarc.fr/>

The risk analysis was performed by generating case-control type data - similar to the INTERPHONE study - based on a sample of 3,000 subjects (1,000 cases and 2,000 controls) for which two mobile phone exposure estimators were available: the “true” exposure and that biased according to the scenario considered. We used a hierarchical Bayesian approach to account for heterogeneity in mobile phone usage data across INTERPHONE study countries.

Results

Our simulation results based on the the most realistic scenarios resulting from the INTERPHONE validation studies show that the

⁸² Statistical model.

⁸³ In statistics, a decile is each of the 9 values that divide a data set into 10 groups of equal numbers.

most likely biased model is fully consistent with the "J" shaped exposure-risk relationship observed in the study

INTERCOM. Although some residual uncertainty remains⁸⁴, data from the INTER-CAL study modify the evaluation

overall, making the causal link between the intensive use of the

mobile phone and an increased risk of glioma.

However, due to the different biases inherent in case-control studies, so-called "prospective" cohort studies are an attractive alternative, providing more solid evidence on whether cell phone use is linked to an increased risk of cancer.

Uses and exposure of children to new technologies

Characterization of the uses and real occasional and cumulative exposure to radio frequencies of communicating mobile devices – including new technologies – in children at different ages

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Research project (ongoing since 2019) - Funding: €399,983 - Contact :

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Key words :	exposure, child,	technology,
	communications, radiofrequency	

In recent years, the uses of mobile phones and connected objects have evolved considerably, especially among children and adolescents. More and more devices are dedicated to them (e.g. radio-controlled toys, game consoles, multimedia glasses, baby monitors) or support specific applications (e.g. video streaming, e-learning): hence the use increase in cell phones for uses other than telephony (e.g. photography, music, sending SMS or "texting", participation in social networks).

While the relationship of children and adolescents to smartphones and wireless devices has evolved, we currently have little objective information on how these devices are used – many studies having focused up

⁸⁴ Samples from validation studies may also be subject to certain biases.

present on the estimation of adult exposure and the assessment of potential risks at the level of the general population.

Social determinants and risk factors

Knowing how cell phones are used (eg telephone, tablet, computer) by children and adolescents could be useful in reducing their exposure. These modalities are multiple; they vary according to social and family contexts, especially since the commercial offers of operators (eg family package, multi-connection) have encouraged the penetration of ICT in French households.



Illustration 20: Virtual reality glasses (Credits: Getty Images)

Recently, surveys like those of Hadopi⁸⁵ have made it possible to characterize, among 8-14 year olds (May 2017), the diversification of their materialized practices. Nevertheless, they intervene in the field of social sciences and, if they highlight the concern of the parents, do not make it possible to study the link between the exposure of young people to radiofrequencies and the possible biological and health effects.

The research project: EXPO-CHILDREN

The main objective of the EXPO project CHILDREN is to identify practices and

to analyze the social determinants of the actual exposure of children (at different ages) to radio frequencies from communicating mobile devices:

1. Collect information and data

on the multiple uses of mobile phones and connected objects in so-called "prospective" cohort studies of children

and adolescents⁸⁶; 2. Study the social determinants of the various devices used

by young people through a bibliographical search by comparing, on the one hand, the offers of mobile telephone operators and, on the other hand, by studying the relationship between the sociological determinants and the prospects for child development;

3. Estimate the exposure of children and adolescents to electromagnetic fields (eg, head, whole body) according to age, emitting device, type of application, as well as the collection of mobile phone usage data and the duration of use.

Methodology

To characterize the exposure of children and adolescents, the project will be based on six existing cohorts of children in three European countries (France, the Netherlands, Poland and Spain) and a new cohort confined to school : • *Children aged 3-6* ○ SEPAGES

(France)⁸⁷ ○ YOUth Baby & child (Netherlands)⁸⁸ ○ Cohort at school (Spain) • *Children aged 9-13*

- EDEN (France)⁸⁹
- INMA (Spain)⁹⁰

⁸⁶ The follow-up period begins on the date the survey is set up. ⁸⁷ <https://sepages.inserm.fr/fr/accueil/> ⁸⁸ Cohort monitored over time : <https://www.uu.nl/en/research/youth-cohort-study> ⁸⁹ <http://eden.vjf.inserm.fr/> ⁹⁰ https://www.isglobal.org/en/project/-/asset_publisher/qf6QOKuKkIC3/content/proyecto-inma-infancia-y-medio-ambiente

⁸⁵ Generation called "native smartphones".

- Cohort at school (Spain) •
Teenagers 14-17 years old
- EDEN (France)⁹¹
- PELAGIE (France)⁹²
- GENERATION R Study (Netherlands)⁹³
- INMA (Spain) ○ REPRO_PL (Poland) ○
School cohort (Spain)

The rat as an animal model study of electromagnetic hypersensitivity

Effect of radiofrequencies (5G, 2 frequencies)
in healthy and depressed subjects: behavioral
and neurobiological approaches to
electromagnetic hypersensitivity (EHS) in rats

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Research project (ongoing since December
2020 - duration: 48 months) - Funding: €293,988
- Contact: pereira@unistra.fr

Key words : electromagnetic hypersensitivity, exposure,
radiofrequencies, electromagnetic radiation, long-term memory,
anxiety, etiology, rat, information and communication
technologies, pain threshold, phenotype, physiopathology,
symptomatology, electromagnetic fields , sex/gender

Electromagnetic hypersensitivity (EHS) is characterized by various symptoms that people attribute to their exposure to electromagnetic fields (EMF). According to the WHO, this hypersensitivity has analogies with other unexplained syndromes such as intolerance to chemical odors (SIOC) or multiple chemical sensitivity (MCS): disorders associated with environmental factors, which, like EHS, remain “medically unexplained and whose effects are detrimental to people’s health ”⁹⁴

⁹¹ <http://eden.vjf.inserm.fr/> ⁹²
<https://www.pelagie-inserm.fr/> ⁹³
<https://generationr.nl/researchers/>

⁹⁴ Quoted in the ANSES report, *Electromagnetic hypersensitivity or idiopathic environmental intolerance to electromagnetic fields*, Scientific Edition, March 2018, p. 4.

Electromagnetic Hypersensitivity (EHS)

The WHO has retained three criteria to characterize EHS⁹⁵ : 1. The subjects' perception of various non-specific functional symptoms⁹⁶ (eg sleep disorders, headaches, skin symptoms); 2. The absence of clinical and biological evidence to explain these symptoms; 3. The attribution, by the subjects themselves, of these symptoms to an exposure to electromagnetic fields, themselves diversified⁹⁷.

Some studies show that people declaring themselves EHS are more anxious and depressed than the average of the general population. But, it is not possible to say if this psychic component is the cause or the consequence of the symptoms felt by these people. In addition, the complaints expressed refer to different sources of exposure: mainly radio frequencies (e.g. mobile phones, Wi-Fi, relay antennas), but also low or extremely low frequencies (e.g. power lines) including modes of interaction with living matter are very different.

An animal model

According to the latest WHO estimates, 5% of adults suffer from depression: ie more than 300 million people in the world⁹⁷ It is one of the main causes of morbidity and disability. The depression translates in particular :

- In men, by weight loss, psychomotor slowing

⁹⁵ *Id.*

⁹⁶ A symptom is said to be "non-specific" when it can express several different diseases.

⁹⁷ Increase of 18% from 2005 to 2015.

and thoughts of self-harm or suicide ; • In women, by increased appetite, pain and gastrointestinal disorders.

This disease affects women more than men. It increases all the more the risk of co-morbidity as it establishes close links with other disorders, in particular anxiety, or non-communicable diseases.



Hypersensibilité électromagnétique ou intolérance environnementale idiopathique attribuée aux champs électromagnétiques

Avis de l'Anses
Rapport d'expertise collective

Mars 2018 Édition scientifique



Figure 21: Electromagnetic hypersensitivity or idiopathic environmental intolerance attributed to electromagnetic fields (ANSES, Scientific Edition, March 2018)

To understand depression, animal models can play an important role. Indeed, affective disorders clearly share many neural mechanisms, which underlie emotions.

In rodents, for example, depression is associated with a set of phenotypes that can be reliably measured (eg change in appetite, decreased concentration, indecisiveness, anhedonia).

Among animal models, FSL98 rats have been shown to be a good genetic model of depression. Like depressed people, they show changes in appetite, loss of energy, sleep disturbances, difficulties in social relations...

controls (Sprague-Dawley rats). These tests target locomotor activity, anxiety, depression, short- and long-term memory, cognitive flexibility, and pain sensitivity. Thus, the study of the cognitive and affective spheres and their neurobiological correlates will be carried out in connection with the phenotype (depressive or not), the exposure to RF and the

The research project: RADIODEP

sex.

The causal relationship between the

Since radiofrequencies and EHS are not scientifically validated, the RADIODEP project proposes to answer the following questions : • Does a depressed person perceive RF differently from a healthy person ?

- Is depression the cause or the consequence of EHS ?
- Is EHS more of a female concern (such as depression, anxiety and somatic complaints)?

This unique approach to EHS in an animal model of depression raises the question of the role of affective (emotional) states in symptomatology and the link with RF. It opens up new perspectives – the absence of an animal model has so far hampered understanding of the etiology and physiopathology of EHS.

Methodology

For the first time, two 5G signals will be studied :

- A low frequency (900 MHz), which penetrates the body ;
- A high frequency (26 GHz), which theoretically does not penetrate.

After the adaptation of a reverberation chamber to 5G signals for the exposure of rats in a breeding cage, behavioral tests will be carried out before, during and after chronic exposure (4 weeks, 5 days/week, 4 hours/day) of male and female FSL rats and their

⁹⁸ From the English " *Flinders Sensitive Line* ".

New approach to measuring brain activity under RF

Functional ultrasound imaging of the brain of rodents under RF exposure

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Feasibility study (from Dec. 2018 to May 2020) – Funding: €49,712 – Contact: delia.arnaud cormos@xlim.fr

Keywords: brain, in vivo, animal experimentation, radiofrequency, ultrasound imaging, electromagnetic radiation, mobile phone, central nervous system, dosimetry, wave absorption, interaction, neuron, echodoppler

A large amount of research has been carried out over the past twenty years to answer the many questions raised by the increasing use of telecommunications systems. But the results are often

contradictory and fail to disentangle the mechanisms of interaction between the neurons and cell phone radiation. How to assess the potential biological effects induced by electromagnetic fields? How to decipher these subtle interactions between living matter and

low level radio frequency (RF)?

A groundbreaking new technique opens up new possibilities for observing *in vivo* (real-time) brain activity and functional connectivity⁹⁹ in mice exposed to radiofrequency radiation.

⁹⁹ Way in which the different regions of the brain interact with each other and form so-called “functional” networks (in English, “*resting state networks*”).

Neuroimaging

Neuroimaging is a recent brain imaging technique; it tracks brain activity through changes in blood flow. Thanks to a new “fUS”¹⁰⁰ method, which marks the introduction of ultrasound into this form of brain imaging, it makes it possible to “image” brain activity in near real time in small animals (e.g. rodents) with high spatial and temporal resolution.

Therefore, our goal is to try to take advantage of this technique during an experimental protocol, to refine the measurements obtained when exposing mice to low-intensity RF.

The research project: RadioFlow

After having improved the “signal” to “noise” ratio of the images, we have exploited a system which makes it possible to “image” the brain of the anesthetized mouse by Doppler ultrasound, that is to say in the least invasive way.

possible¹⁰¹. Thus, the main objectives of our project are:

1. The development and characterization of a “head-only” system for recording the brain activity of mice during their exposure to radiofrequencies;
2. Carrying out preliminary tests to assess the effectiveness of this new application for monitoring the brain activity of mice;
3. Obtaining, from *in vivo investigations*, preliminary results on this cerebral activity during exposure to RF.

¹⁰⁰ From the English “*functional ultrasound imaging*”.

¹⁰¹ Without major surgery and injection of agents contrast.

Methodology

A new experimental system has been designed to simultaneously allow :

- Exposure of “head only” mice to RF fields using a dipole¹⁰² (or dipole antenna) ;
- Recording of

the activity cerebral with an ultrasound probe (fUS) developed by the startup Iconeus¹⁰³

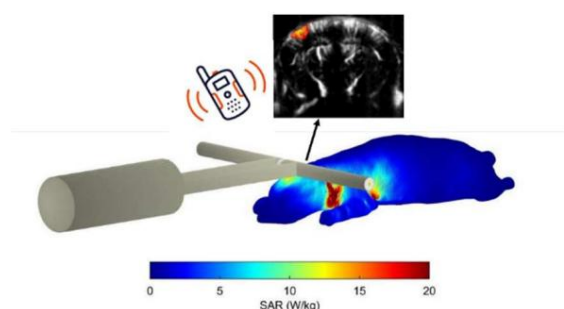


Figure 22: Tracking mouse brain activity during RF exposure (Credits: XLIM-IMS)

To provide a complete and precise dosimetry of the interaction between the electromagnetic field generated by the antenna and the mice, three "phantom" models have been used and characterized, with increasingly realistic shapes: flat rectangular, simplified mouse and mouse shape.

The specific absorption rate¹⁰⁴ (SAR) of the exposure system was evaluated using experimental temperature measurements and numerical electric field simulations. Based on dosimetry, exposures were made at SAR values of 2W/kg, 6W/kg, CW¹⁰⁵ and GSM¹⁰⁶.

¹⁰² Antenna made up of two metal strands, fed in the middle to transmit (or receive) electromagnetic energy: adapted, here, to the considered frequency of 1.8 gigahertz (GHz).

¹⁰³ Website: <http://iconeus.com> ¹⁰⁴ Or SAR in English “ Specific Absorption Rate ”.

¹⁰⁵ From English “ continuous wave ” for continuous wave: electromagnetic wave of amplitude and frequency constants.

Results

For the first time, we evaluated in this study, the possibility of analyzing real-time cerebral responses of mice during RF exposure. This work constitutes a fundamental first step for further study of the interactions between RF and the central nervous system.

Analysis of the results obtained at 6 W/kg clearly shows no impact of exposure on the response evoked in the primary sensory cortex¹⁰⁷ left "S1HL", after contralateral whiskers and the cortex activity

average functional. The additional results at 2W/kg will also be the subject of an in-depth analysis.

We plan to continue our efforts to assess the effects of RF on the brain activity of awake mice and provide valuable information, especially when studying new signals.

Publications:

R. Orlicchio, Y. Percherancier, F. Poulletier de Gannes, A. Hurtier, I. Lagroye, P. Leveque, D. Arnaud-Cormos, “In Vivo Functional Ultrasound (fUS) Real-Time Imaging of Mice Brain Under Radiofrequency Exposure”. *Bioelectromagnetics*, April 2022.

¹⁰⁶ From the English “ Global System for Mobile Communication ”, digital standard for mobile telephony.

¹⁰⁷ Primary sensory cortex, hind limbs. Of English, “ Primary sensory cortex hind limb ”.

Variation of the intracerebral effects of radiofrequencies according to the state of health

Effects of 2G and 4G mobile radio frequencies on activated microglia and the activity neuronal in context neuroinflammatory

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Keywords: inflammation, central nervous system, brain, neuron, microglia, cell culture, radiofrequency, mobile telephony, wave absorption, biological effect, health risk, neurotransmission, electrophysiology, animal model, rat, mouse, modeling, *in vivo*, *in vitro*, messenger RNA, cytokine, histone

Neuroinflammatory states are important components of many pathologies with resolving or progressive characteristics and which directly or indirectly affect the central nervous system (CNS). These include neurodegenerative or metabolic diseases, certain viral or bacterial infections, epilepsy, psychiatric conditions, vascular accidents, brain tumors, or traumatic damage to the CNS. These neuro-inflammatory reactions

involve morphological and functional modifications of cerebral cells, which influence the activity of neuronal networks and which can promote or, on the contrary, limit the emergence or development of cerebral lesions.

Activation of microglia

Present in all structures of the CNS, microglia cells are part of the so-called “innate” immune system. Activation of microglia occurs in pathologies affecting the CNS and it plays a key role in the development and control of neuroinflammatory reactions.

Good his Although characteristics vary by pathological background, microglia activation typically involves enlargement or changes in the cells' ability to produce inflammatory mediators.

The research project: 2-4Ginf

Our working hypothesis is that the sensitivity or response of brain cells to RF may vary depending on the health status of the exposed subjects. The work presented here is based on *in vivo* or *in vitro* animal models

compatible with analyzes at the cellular and molecular levels, which makes it possible to better understand the biological effects of RF and their possible health impacts. They follow previous studies¹⁰⁸, which showed that, in rats subject to acute neuro-inflammation, exposure of the head to GSM-1800 MHz (2G) type RF could cause transient changes in cell morphology. microglia and neurotransmission.

These observations prompted further analysis of the effects of GSM signals on key cells of neuroinflammation such as microglia and they raised the question of the effects of other electromagnetic signals used by mobile telephony, on individuals subject to neuroinflammatory states. .

¹⁰⁸ Neurinf 1800 (2015-RF-12) and Microg-1800 (2013-RF-03) projects funded by PNR EST. See Michel Mallat. Effect of GSM 1800 MHz signals on the central nervous system: Effect of GSM 1800 MHz waves on cells microglial cells and neurotransmission in a neuroinflammatory context. *The Research Papers. Health, Environment, Work*, ANSES, 2017, Radiofrequencies and health, pp.26-28. yhandles-01791399j

Goals

Our project aimed to investigate *in vivo* the effects of LTE -1800 MHz (4G) signals on the electrical activity of neurons and the morphology of microglia in the context of an acute neuroinflammatory episode. A second part aimed in particular to deepen the characterization of the effects of GSM 1800 MHz signals on microglia according to the state of cell activation, by using cell cultures (*in vitro approach*).

Methodology

The *in vivo* analyzes were carried out on rats subject or not to an acute neuroinflammatory state¹⁰⁹ and exposed to LTE-1800 MHz (4G) signals lasting 2 hours and of limited incidence to the head. They included the determination of the powers absorbed by the cerebral tissue (SAR: specific absorption rate), an electrophysiological analysis of the activity of the neurons and a study morphology of microglia carried out in the auditory cortex¹¹⁰



Figure 23: Culture plate (24 wells) inserted into a device housed inside a culture incubator. The device's power supply allows calibrated exposure of microglial cells seeded in culture wells to 1800MHz GSM-type signals (Credits: Michel Mallat)

The *in vitro* analyzes exploited a system designed for the exposure of cell cultures to GSM signals, and applied to cells

¹⁰⁹ Induced by lipopolysaccharide (LPS) treatment.

¹¹⁰ Level from which analyzes of neural activity were performed.

microglia purified from normal mouse brains. The microglial cultures were subjected or not to treatments with chemical activators before and during exposure to GSM signals. The analyzes focused on the microglial expression of epigenetic marks (proteins associated with DNA of the methylated or acetylated histone type) or of genes coding for inflammation mediators (cytokines, enzymes), by quantification of protein levels, enzymatic activities or corresponding messenger RNAs.

Results

• *In-vivo* studies

The *in vivo* observations related to the auditory cortex of rats at the level of which the mean SAR resulting from exposure to LTE signals reached the value of 0.5 W/kg. In rats subject to an acute neuroinflammatory state, exposure to LTE signals caused changes in the electrical activity of neurons with a reduction in the strength of the response evoked by pure tones or by natural vocalizations, as well as an increase in the response evoked by pure tones at the low and mid frequencies, which appear between 3 and 6 h after the end of the exposure. These changes occurred in the absence of a change in the scope of the

cortical areas occupied by cell bodies and extensions of microglial cells. In healthy rats, the same exposure to LTE signals did not cause changes in acoustic thresholds or the strength of neuronal responses induced by sound stimuli.

• *In vitro* studies

It appeared that the *in vitro* exposure of purified microglial cells to signals GSM-1800 MHz may cause increases or decreases in intracellular levels of messenger RNAs coding for

cytokines involved in neuroinflammatory reactions or for enzymes producing reactive oxygen forms or catalyzing the demethylation or deacetylation of histones. These changes in RNA levels have been observed in

cells activated by a proinflammatory agent such as lipopolysaccharide. They occur in response to exposure to GSM signals lasting 15 h with SAR values equal to or greater than 0.65 W/kg. No reproducible modification was observed in the level or in the enzymatic activity of the proteins tested. The functional impact of these messenger RNA modulations therefore remains uncertain. Furthermore, mRNA levels remained unchanged in microglial cultures exposed to GSM signals in the absence of cell activating treatment.

Findings

Our work shows changes in neuronal activity or expression of microglial genes induced by LTE- or GSM-1800 MHz signals, in experimental contexts that model acute neuroinflammatory reactions. They support the hypothesis of an increase in the sensitivity of brain cells to GSM or LTE signals during reactions

neuroinflammatory. However, them reported changes have been observed in response to prolonged exposures and SAR values (\bar{y} 0.5 W/kg) that remain higher than those assessed in the human cerebral cortex in situations of mobile phone use. .

Publications:

Souffi S, Lameth J, Gaucher Q, Arnaud-Cormos D, Lévêque P, Edeline JM, Mallat M. Exposure to 1800 MHz LTE electromagnetic fields under proinflammatory conditions decreases the response strength and increases the acoustic threshold of auditory cortical neurons. *Sci Rep* 12, 4063 (2022) <https://doi.org/10.1038/s41598-022-07923-9>

Prenatal exposure to WiFi

Prenatal exposure to Wifi-type radiofrequency signals: effects on neuronal development and adult behavior in mice

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Research project (from January 2019 to June 2022)
– Funding: €199,680 – Contact :

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Keywords: neuron, animal experimentation, dosimetry, radiofrequency, prenatal exposure, mouse, central nervous system, child, newborn

Following the significant development of radio frequency (RF) technologies, law No. 2015-136 known as the “Bee” law¹¹¹ lays down the principle of sobriety in the face of public exposure to electromagnetic waves. It aims to protect children in particular, by prohibiting Wi-Fi in areas dedicated to reception, rest and activities in collective establishments welcoming children under the age of

three years. However, few data are available on the effects of Wi-Fi exposure occurring in early life or during gestation. On the one hand, this raises public concern and, on the other, requires additional research into the potentially dangerous health effects of this type of exposure. Due to the proximity of mobile phones to the head, it is the central nervous system (CNS) that is the subject of the greatest questions.

¹¹¹ Law No. 2015-136 promulgated on February 9, 2015 (under the impetus of the deputy Laurence Abeille) relating to sobriety, transparency, information and consultation in terms of exposure to electromagnetic waves.

brain development

From the first months of pregnancy, the brain begins to form and evolve.

During embryonic life, a few thousand neurons are born, migrate and differentiate; they must communicate with each other (interconnect) for the brain to function. A defect in the formation of neural circuits¹¹² and/or in the organization of the brain can lead to cognitive impairments and an increased susceptibility to major psychiatric and neurological alterations such as attention deficit disorder (hyperactivity), spectrum disorders autism or schizophrenia.

However, certain studies conducted in mammals show that genes and the environment act in concert during periods of increased sensitivity (eg prenatal period, early childhood, adolescence).

The research project: WIFIDEV

Since we are almost constantly exposed to Wi-Fi signals, our project aimed to assess the effect of these exposures on embryonic development as well as brain development and functioning in adulthood. To do this, we used male and female outbred mice as a study model.

preferential because the basic mechanisms of brain development, cell distribution and brain maturation are comparable to those of the human brain.

Methodology

Mice were exposed to Wi-Fi type RF continuously, 24 hours a day, from the first day of gestation to the twenty-first day after birth – this period covering

¹¹² At birth, a newborn's brain already has around 100 billion neurons.

the main phases of brain development:

- The exposure equipment had two exposure cages, one used for signal exposure Wi-Fi and the other acting as a witness¹¹³ ;
- Adjustments and calibration of exposure levels were made to ensure the desired Specific Absorption Rate (SAR) values, i.e. 0.08 W/kg whole body¹¹⁴ • Development of the cortex brain and associated processes were characterized to assess :
 - The impact of Wi-Fi exposure on neuronal development processes ;
 - The developmental consequences of neuronal architecture, which plays a key role in the connectivity of future neurons; Behavioral consequences in adulthood using paradigms targeting motor functions, anxiety, social interaction as well as certain aspects of depression and learning and memory abilities.

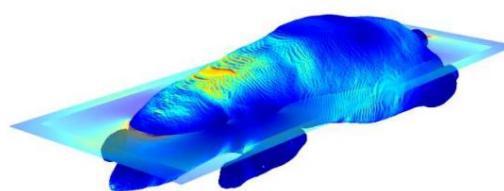


Figure 24: Example of Absorption Rate Specific (SAR) and electromagnetic field mapping (horizontal plane) when exposing a mouse model to a Wi-Fi type signal of 2.45 GHz (Credits: Philippe Lévêque, Xlim, CNRS University of Limoges)

¹¹³ No RF.

¹¹⁴ For a mouse weighing 20 to 25 grams, the generator and the amplifier were set to generate an electric field in the exposure zone around 20V/m (value consistent with the reference values for exposure in man: 61 V/m effective for a SAR of 0.08 W/kg whole body).

Results

Our work did not reveal any significant positive or negative effects of Wi-Fi type RF either on the weight of the pregnant female, the sizes of the litters, the male/female ratio or the growth of the pups, nor on the development of their brains and behaviors in adulthood. Given these results, we do not recommend any change in current population protection standards.

However, if no direct risk seems to appear in normal mice (without comorbidities), exposure to Wi-Fi signals could constitute a risk for people weakened by an environment or genetics at risk. A similar behavioral analysis could be performed in animals already having mild developmental pathology or undergoing, for example, chronic stress.

DNA damage and millimeter waves

DNA damage response pathway analysis in response to co-exposure including millimeter waves

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Feasibility study (from Nov. 2019 to Oct. 2021) -
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Keywords: multiple exposure, radio frequency, electromagnetic radiation, millimeter wave, exposure, information communication technology, genotoxicity, cell, DNA, oxidative stress, feasibility study, technology, communication, telecommunication,

The use of radio frequency (RF) technologies and associated services (mobile applications, audio and video *streaming*, social networks, etc.) leads to the saturation of existing frequency ranges and requires the use of higher carrier frequencies, including 5G¹¹⁵ technology and millimeter waves. In France, it is planned to exploit two new frequency bands (3.5 GHz and 26 GHz), the upper limit of this spectrum of frequencies the millimeter waves, little telecommunications studied, even less than the RF regarding their safety.

DNA repair

In response to societal concerns, many research teams have studied the effects of RF likely to compromise

¹¹⁵ Fifth generation.

the physical or functional integrity of the genome (genotoxicity). Although no lasting effect " *on the loss of DNA integrity has(was) demonstrated under thermal conditions* ", the ANSES experts recognize that "it is not impossible that under certain conditions, RF induces DNA breaks (...)

Nevertheless, the latter are often of low magnitude (close to the natural background noise) and are probably quickly repaired. They are probably of no consequence for the integrity of the chromosomes. »¹¹⁶



Illustration 25: Radiofrequencies and health (ANSES, Oct. 2013)

These findings suggest that DNA repair systems are efficient enough to manage the alterations suffered during RF exposure. Thus, if the hypothesis of a relationship between exposure, oxidative stress

and genotoxic effect¹¹⁷ is true, then the damage caused is not numerous enough to overwhelm the self-healing capacity of the cells.

However, from the point of view of risk analysis, it now remains to confirm that the repair systems are indeed mobilized under exposure and to assess the impact that this exposure could have on people with genetic defects in certain of these systems.

millimeter waves

The waves millimeters (WMO) correspond to frequencies between 30 and 300 GHz¹¹⁸. Compared to radio frequencies, the energy transmitted to the body is absorbed very locally. This implies that the depth of penetration of these waves is lower and its corollary, that exposure to OMMs induces on the surface of the body, a much higher specific absorption rate (SAR).

The biological effects of OMMs can be divided into two categories: thermal effects (proven) for high-power radiation and non-thermal effects (still controversial) at lower power. At certain intermediate power levels¹¹⁹, these waves are used in countries of the former Soviet Union. This suggests that interactions are possible between OMMs and living organisms.

Before the massive use of these new communication technologies by the general public, it was necessary to check whether or not exposure to OMMs could cause DNA damage, repair them, etc.

¹¹⁶ *Radiofrequencies and health*, ANSES Opinion, October 2013.

¹¹⁷ Hypothesis put forward by *Kesari et al.*

¹¹⁸ From 1 mm to 10 mm in terms of wavelength. ¹¹⁹

At the limit of thermal effects from 5 to 15 mW/cm².

¹²⁰ Ranges used: 42.2 GHz, 53.6 GHz and 61.2 GHz.

The research project: CoExpO

By using innovative approaches and methodologies, our project was to provide additional knowledge on the biological or health effects of OMMs, prior to their deployment in the general public. It thus responded to ANSES's priority themes: taking into account “changes in the use of frequencies linked to new uses and new communication technologies. »

The objective was to carry out a pilot study lasting one year, in order to verify whether it was necessary to study in more detail the impact of OMMs on the response to nuclear DNA damage when there is co-exposure with genotoxic stress¹²¹ .

Methodology

Our work focused on :

- Damage induced by DNA double-strand breaks because these are high-risk lesions (carcinogenic) ;
- Damage produced by oxidative stress because it is very frequent and also affects DNA replication.

Three cell lines were used *in vitro* :

- Two lines of human skin cells because this organ is the preferred target of OMMs ;
- A “U2OS ”¹²² tumor cell line classically used in the study of DNA damage signaling pathways and their repair. • Finally, the cells were placed in an incubator at 37°C and exposed to a frequency of 60 GHz as

previously described¹²³. For the majority of the experiments, the incident power density corresponded to the maximum exposure authorized by the standards currently in force, ie 1 mW/cm² .

Results

A first series of experiments shows that acute exposure to OMMs does not induce DNA damage requiring the activation of damage response signaling pathways. Similarly, the consortium did not demonstrate any potentiating effect of the waves on these signaling pathways, which seems to indicate that OMMs are not co-genotoxic either.

These results are close to those obtained by numerous *in vitro* studies on RF. They will need to be confirmed by more sensitive detection methods. Because, by using very sensitive techniques, never used until now for this type of study, the consortium has shown that there could be an effect of OMMs on the ability of cells to repair double-strand breaks in the DNA in a co-exposure context.

The results obtained being significant, but weak in terms of effect, it will be necessary to repeat these experiments to confirm them and properly characterize the phenomenon. In the end, it therefore seems that the switch to higher frequencies does not radically change the situation with regard to the direct dangerousness of exposure, but additional studies, using very sensitive methods will be necessary. to confirm.

¹²¹ In general, to acquire detailed and clear knowledge, the effect of one stress “at a time” is studied. In reality, cells are often subjected to the action of several stresses to which they must respond and/or adapt.

¹²² Human osteosarcoma.

¹²³ Alexis J. Haas, Yann Le Page, Maxim Zhadobov, Artem Boriskin, Ronan Sauleau and Yves Le Drean. Impact of 60-GHz Millimeter Waves on Stress and Pain-Related Protein Expression in Differentiating Neuron-Like Cells. *Bioelectromagnetics* 37:444-454 (2016)

The adaptive response to radio frequencies

Adaptive response to radiofrequency fields: is autophagy the key ?

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Research project (from January 2018 to February 2021) – Funding: €251,160 – Contact : muriel.priault@ibgc.cnrs.fr

Keywords: radiofrequency, electromagnetic field, adaptive response, autophagy, comet test, neuroblastoma, tumor cell, cell

The effects of radio frequency (RF) on the health of the public have been the subject of multiple studies giving very eclectic results.

For the moment, no genotoxic effect (DNA damage) of RF has been demonstrated. ADAPT instead explores the possibility that RF preconditioning may protect against DNA damage if the model is exposed to genotoxic agents.

autophagy

Considered as an essential physiological process, autophagy occurs at the cellular level in response to various stresses (eg oxidative stress, nutritive stress, viral or bacterial infection). It is an intracellular mechanism that degrades and then recycles non-essential or damaged cellular components to protect cells.

To assess the potential protective effects of RF, human cells were exposed in the laboratory to GSM-900 signals combined with treatment with an oxidizing agent, menadione (MD) producing

genotoxic effects. A decrease in genotoxic stress was observed by comparison with cells not pre-exposed to RF: this is the adaptive response (AR). As the molecular mechanism of AR remains

unknown, this experimental system opens the possibility to explore whether autophagy was triggered during AR.

The research project: ADAPT

Given the variability of the results obtained in the field of RF and bioelectromagnetism, we wanted to test whether a beneficial effect could be observed: in particular, by stimulating a stress response (or autophagy).

The objectives consisted, in order of importance, of: 1. Getting two laboratories to independently reproduce the adaptive response observed following the cumulative “RF+menadione” exposure of SH-SY5Y cells;

2. Determine if autophagy is the signaling pathway implemented in the adaptive response; 3. Determine the role of oxidative stress (ROS) in the adaptive response; 4. Explore *in vitro* and *in vivo* new parameters for setting up the adaptive response.

Methodology

The *in vitro* parameters for which an adaptive response was systematically observed are as follows:

Cellules	SH-SY5Yensemencées à 800 000 cellules par puits
Durée/fréquence d'exposition	Pendant 3h (48h après ensemencement)
	Pendant 10h (48h après ensemencement)
	De 53h à 63h après ensemencement
RF	1h par jour sur 3 jours (dès 24h après ensemencement)
	1950 MHz, UMTS, DAS 0,3 W/kg
Ménadione	1950 MHz, UMTS, DAS 1,25 W/kg
	10 µM pendant 1h avant récolte

Results

Although the two laboratories followed the same experimental protocol, they did not manage to obtain the same results. Moreover, measurements of autophagic activity do not show any significant difference between cells exposed to RF alone or cells pre-conditioned to RF and exposed to menadione. On the other hand, if autophagy is inhibited, the adaptive response is no longer observed, which indicates a link between these two phenomena.

The results obtained by this research project therefore confirm the great variability of the biological phenomena measured in response to radiofrequencies.

The question of the involvement of autophagy in the adaptive response requires new, more in-depth studies to more fully document the arguments.

Publications:

Inhibition of Autophagy Negates Radiofrequency Induced Adaptive Response in SH-SY5Y Neuroblastoma Cells.

Sannino A, Scarfi MR, Dufossée M, Romeo S, Poeta L, Prouzet-Mauléon V, Priault M, Zeni O. Int J Mol Sci. 2022 Jul 29;23(15):8414. doi: 10.3390/ijms23158414. PMID: 35955556

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Abbreviations used

3GPP, From the English “3rd Generation Partnership Project” (consortium)

5G, Fifth Generation

Afsset, French Agency for Environmental and Occupational Health Safety

ANFR, National Frequency Agency

ANSES, National Agency for Food, Environmental and Occupational Health Safety

Arcep, Regulatory Authority for Electronic Communications, Posts and Distribution of
hurry

BRET, From the English “Bioluminescence Resonance Energy Transfer »

CEA, Commissariat for Atomic Energy and Alternative Energies

EMC, Electromagnetic Fields

IARC, International Center for Research on cancer

CNRS, National Center for Scientific Research

C-V2X, From the English “cellular vehicle to X”

CW, From the English “continuous wave” (wave continues)

D-2HG, D-2 hydroxyglutarate (oncometabolite)

SAR, Specific Absorption Rate

EA, Home Team

ELF, Extremely Low Frequency

EHS, From English “Electromagnetic electromagnetic hypersensitivity (hypersensitivity)

FSL, From English “Flinders Sensitive Line”

fUS, From the English “functional ultrasound imaging”

GHz, Gigahertz

GPS, From the English “Global Positioning System” (navigation assistant)

GSM, From the English “Global System for Mobile Communication” (2G)

CI, Confidence Index

Icnirp, International Commission on Non-Ionizing Radiation Protection

INCa, National Cancer Institute

Ineris, National Institute for the Industrial Environment and Risks

INRAE, National Institute for Agronomic Research

INRS, National Institute for Research and Security

Inserm, National Institute for Health and Medical Research

IoT, From the English “Internet Of Things” (Internet of Objects)

Itmo, multi-organization thematic institute

ITS, From the English “Intelligent Transport System” (Intelligent Transportation System or ITS)

LPS, Lipopolysaccharides

LTE, From the English “Long Term Evolution”

MAP, From the English “Mitogen-activated protein”

MMS, From English “Multimedia Message Service ”

OMM, Millimeter wave

WHO, World Health Organization

ONIE, Non-ionizing electromagnetic waves

OR, Odds ratio (odds ratio or odds ratio)

PNR EST, National Research Program in Environment-Health-Work

PST, Occupational health plan

RAS, From English “Retrovirus Associated Sequences »

RF, Radiofrequency

**ROS, from English "Reactive oxygen species"
(Reactive Oxygen Species)**

**S1HL, Primary Sensory Cortex, hind limbs. From English,
"Primary sensory cortex hind limb"**

**SCENIHR, Scientific Committee on Emerging and New
Health Risks**

SCM, Multiple Chemical Sensitivity

SMS, From English "Short Message Service"

CNS, Central Nervous System

ALS, Amyotrophic Lateral Sclerosis

TRP, From English "Transient Receptor Potential"

UMR, Joint Research Unit

**UMTS, From English "Universal Mobile
Telecommunications System" (3G)**

WiFi, From the English "wireless fidelity "

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ACTUALITÉS

L'EXPOSITION DES ENFANTS (01/12/2021)

Dans ce nouveau numéro des Cahiers de la Recherche sont appréhendés non seulement les mécanismes épigénétiques mais aussi les facteurs de risque qui peuvent, au cours de fenêtres précoces de vulnérabilité (vie fœtale, petite enfance...) avoir des conséquences sur la santé ultérieure de chaque individu tels l'exposition à des produits chimiques, à une alimentation déséquilibrée ou bien à un stress psychosocial, composantes que l'exposome cherche à capter dans une approche intégrative.

Depuis décembre 2012, les Cahiers de la Recherche (Santé, Environnement, Travail) forment une collection thématique, qui dresse un panorama des projets de recherche financés dans le cadre du Programme National de Recherche Environnement Santé Travail (PNR EST).

Ces projets traitent de questions de sécurité sanitaire qui, souvent, interpellent l'opinion publique. Ces questions sont associées à des agents physiques, biologiques ou chimiques, présents dans l'environnement ou dans le milieu professionnel. Parmi eux, les nanomatériaux, les radiofréquences, et de nombreuses substances chimiques. Les interrogations qui leurs sont associées sont multiples depuis la mesure de l'exposition des personnes à celle de la caractérisation de leurs effets. Traiter de ces sujets mobilise des équipes pluridisciplinaires (biologie, écotoxicologie, épidémiologie, médecine, sciences humaines et sociales...) qui collaborent sur des projets de recherche, visant à améliorer les connaissances. On attend de ces nouvelles connaissances qu'elles contribuent à mieux évaluer des risques et puissent ainsi éclairer la prise de décisions publiques pour la gestion des risques.

Le but des Cahiers de la Recherche est d'explicitier les questions que se posent les scientifiques en amont de leurs projets, et de donner des exemples de résultats qu'ils peuvent ainsi produire.

RECHERCHE

Termes de recherche (" pour tous) [Rechercher]

MOTS CLÉS

Nanoparticule Bisphénol A Inflammation Pollution atmosphérique
Indicateur Pesticide Alimentation Rhinite Interaction Épidémiologie
Facteur Risque Tumeur Médicament antibiotique Méthode alternative
Perturbateur endocrinien Toxicité Bactérie
Exposition Système nerveux central Air intérieur Contamination
Exposition maternelle In vitro Adipose Appareil respiratoire Foie Dioxide de
stane Enquête cas témoin Arbovirose Inhalation Agriculture Rayonnement
électromagnétique Téléphone mobile Enfant Polluant organique persistant Poussière
Stress oxydant Radiofréquence Microorganisme Cancer Dissémination
Insecticide GÈNE Composé chimique Antibiorésistance Vulnérabilité Translocation
Substance active Eau usée Résistance Prévention Persistance Mécanisme action
Cellule Dose faible Poumon Lutte contre moustique Adiposité Solvant Jedis
allopictus Formaldéhyde Station épuration Arbovirose Exposition
professionnelle Produit chimique Toxicologie Phalax
Amiame Génomique Métabolite Escherichia coli Biocide Particule atmosphérique
Environnement Leucémie Mélange Qualité air Barrière Silex Métrologie Mesure
Élevage Pyréthroïde Exposition multiple Polluant Métabolisme Moustique
Grossesse Nanotechnologies Biomarqueur Marne emploi exposition
Modélisation Particule fine Allergie Champ électromagnétique Carreau Trafic
Modèle Cohorte Hydrocarbures aromatiques polycycliques

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