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CHAMPS ÉLECTROMAGNÉTIQUES :
DE LA DOSIMÉTRIE À LA SANTÉ HUMAINE

Téléphones mobiles, lignes électriques et cancer : les évidences épidémiologiques menant à la classification comme cancérigènes possibles

Mobile phones, power lines and cancer: the epidemiological evidence leading to classification as possible carcinogens

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Résumé

There is still an ongoing scientific controversy whether exposure to electromagnetic fields (EMF) is associated with an increased cancer risk in humans. Epidemiological studies have shown a consistent association between exposure to extremely low-frequency (ELF) magnetic fields and the risk of leukaemia in children, but even after decades of investigations it is unclear whether the observed association is causal or due to bias and limitations of the studies. The International Agency for Research on Cancer (IARC) has therefore classified ELF magnetic fields as possibly carcinogenic to humans. Several studies of different designs investigated the association between radiofrequency (RF) electromagnetic fields related to the use of mobile telephones and the risk of brain tumours. While short-term use of mobile phones of less than ten years was not related to any increased tumour risk, uncertainty remains particularly for longer term heavy users. Mobile phone studies are methodologically challenging and future study protocols need to reduce limitations observed in studies available today. In 2011, IARC has also classified RF EMF as possibly carcinogenic to humans, based on epidemiological studies showing some indications for glioma or acoustic neuroma.

Introduction

Exposure to electric, magnetic and electromagnetic fields in low and high frequency ranges is ubiquitous in modern society. Consequently, even small health risks could have large effects on a population level, as exposures are so widespread. Regarding extremely low-frequency (ELF) magnetic fields there is little evidence for any increased cancer risk, except the observation of an increased risk of childhood leukaemia at exposure levels of 0.3-0.4 □T or higher. Based on these observations, in 2002, the International Agency for Research on Cancer has classified ELF magnetic fields as a possible carcinogen. In recent years research has focused on radiofrequency (RF) electromagnetic fields emitted from mobile phones and, as the devices are held directly to the head, specifically investigated the risk of different types of brain tumours. The IARC classification of RF as possibly carcinogenic to humans was performed in May 2011. Since then, several large epidemiological studies have been published.

1. ELF magnetic fields and the risk of leukaemia in children

Childhood cancer under the age of 15 years is rare accounting for less than 1% of all neoplasms diagnosed each year in developed countries. Acute leukaemias are the most common malignancy in children, accounting for a third of all diagnoses. The incidence rate of acute leukaemias ranges from 30-50 per 1 million children per year. The most recent data on incidence trends indicate a small annual increase of 0.7% in European countries in the last three decades *(Steliarova-Foucher et al, 2000),* however, some of the increase is likely to be attributable to progresses in childhood cancer classification and registration. The biological heterogeneity of childhood leukaemia is well documented and it is therefore unlikely that there is a single causal exposure or mechanism (*Biondi et al, 2000*). Little is known about the aetiology of childhood leukaemia; only few genetic predispositions and high doses of ionizing radiation have been established as risk factors. ELF magnetic fields have been studied as a risk factor for childhood leukaemia since the late

1970s. At present, more than 20 epidemiological studies have investigated this topic, with significant improvements in study designs and methods of exposure assessment over time. These studies have been pooled in separate meta-analyses. Greenland *et al*. pooled all available studies, however, they had to combine various exposure indices into one single metric. They reported a combined relative risk estimate for leukaemia of 1.7 (95% confidence interval (CI) 1.2-2.3) in children exposed to average magnetic fields above 0.3 μT compared to those exposed below 0.1 μT *(Greenland et al, 2000*). Ahlbom et al (*2000*) only pooled studies that fulfilled certain inclusion criteria such as a defined population base for case ascertainment and control recruitment and usage of long term measurements or historical magnetic field calculations for exposure assessment. They reported a relative risk estimate of 2.0 (95% CI 1.3-3.1) for exposures > 0.4 μT compared to exposures < 0.1 μT. More recently, studies published after these first meta-analyses were gathered and pooled by Kheifets et al. confirming the association shown in the previous pooling projects (*Kheifets et al, 2010).* Particularly in studies measuring magnetic fields participation rates were low, thus, the study populations might have been not representative to investigate the association. Simulation studies using the dataset of the German study suggest that 66% of the observed association were attributable to bias and error (*Schüz et al, 2007*). This suggests an overestimation of the strength of the association, but raises the question whether bias explains the association in its entirety (*Schüz et al, 2008*).

2. Mobile phone use and the risk of brain tumors

Glioma and meningioma are the most common types of brain tumours in adults. Glioma, comprising mainly highly malignant tumours with poor prognosis, occur more often in men, with incidence rates between 2-4 per 100,000 men in 20-39 year olds, 8-10 per 100,000 in 40-59 year olds, and around 15 per 100,000 in 60-79 year olds; respective incidence rates in women are 2-3, around 5 and around 10 in the according age groups. Meningioma, a benign brain tumour, occurs more often in women, with incidence rates of 1-2/100,000, 4-8/100,000 and 10-15/100,000 in the 20-39,40-59 and 60-79 year olds, whereas respective rates in men are low with <1, 2-3 and around per 100,000. Overall, incidence rates of brain tumours have been rising over the last decades, mainly attributable to a 50% increase of meningioma in women above age 50 years. If mobile phone use causes brain tumours, the marked increase in prevalence of use over a 20-year period will eventually influence the time trends of the incidence rates of these tumours. Studies of the time trends in the incidence rates of brain tumours among adults have been published in the Nordic countries (*Deltour et al, 2009, Deltour et al, 2012*), in England (*de Vocht et al, 2011*), and in the USA (*Inskip et al, 2010, Little et al, 2012*). No clear trend change was observed in the last years of observation. Recent publications (*Deltour et al, 2012, Little et al, 2012*) have assessed the lack of compatibility between the generally constant incidence rates of gliomas and markedly raised odds ratios reported in some Swedish case-control studies, pointing to biases and errors as at least part of the explanations of the Swedish raised ORs.

In Denmark, a cohort study included all Danes aged more than 30, and born after 1925, subdivided into early subscribers (358,403 persons) and non–subscribers of mobile phones before 1995 (*Frei et al, 2011*). They were followed up for cancer incidence until end of 2007. The risk of central nervous system tumours was not increased in men (incidence rate ratio 1.02, 95% confidence interval 0.94 to 1.10, based on 714 early subscribers cases compared to 4397 cases in the rest of the cohort) and in women (IRR =1.02, 95% confidence interval 0.86 to 1.22, based on 132 early subscribers cases compared to 5486 cases in the rest of the cohort). Among men who had subscribed more than 13 years ago, the risk of glioma was 0.98 (95% confidence interval 0.70 to 1.36, based on 37 early subscribers cases compared to 1853 cases in the rest of the cohort). There is no association between duration of mobile phone use up to 13 years, and risk of adult brain tumours in this dataset.

A multinational case control study with adult cases of brain tumour and acoustic neuromas, and their matched controls ("Interphone") was conducted in 13 countries *(Interphone Study Group, 2010, 2011).* The analyses of 2708 glioma and 2409 meningioma, and equivalent number of controls showed little indications of increased risks for meningiomas, but an increased risk of glioma among those who reported using their phone more than 1640 hours (Odds Ratio 1.40, 95% CI 1.03 1.03–1.89). The analyses of 1105 acoustic neuroma cases showed an OR of 2.79, (95%CI 1.51-5.16) when 5 years latency were postulated. A case-case study conducted in Japan on 787 cases, indicated also a increased risk of 3.08 (95%CI 1.47-7.41) for those who called more than 20 minutes per day on average, 5 years before diagnosis, but there were indications of detection and recall bias in this group (*Sato et al, 2010*).

A case-control study of brain tumours in children aged 7 to 19 years old was also conducted in Denmark, Norway, Sweden, and Switzerland, and these results will be reported (*Aydin et al, 2011*).

3. Conclusion

Electromagnetic fields remain an exposure of high public concern. Mobile phones are still a relatively recent technology, thus, given usually long induction periods of cancer further research is warranted. Shorter term use, i.e. not longer than 10-15 years, does not appear to be related to any substantial brain tumour risk, as time trends in incidence rates have been stable, cohort studies showed no associations, and case-control studies showed at most modest risk increases in sub-groups that might well be attributable to methodological limitations. Prospective cohort studies are recommended to be the way forward, to overcome these limitations and a large prospective cohort study of adults, the

Cosmos study, investigating heavy and long term mobile phone use and the risk of neoplasms, neurological diseases and symptoms, is ongoing in 5 countries, and a feasibility study is on-going in France (Schüz et al, 2010). Objective traffic data from networks operators is recorded, together with self-reported use of mobile phone.

Whether the association between ELF magnetic fields and childhood leukemia is causal remains a scientific controversy; although the epidemiological evidence is consistent, no plausible mechanism to explain the observed association has been proposed so far. If the association is causal, it is estimated that about 1% of all childhood leukaemia would be attributable to ELF magnetic fields in Western European countries while this proportion would be 2-3% in North America, with little data for profound estimations in other parts of the world. It is unlikely that further epidemiological studies will enhance the field and the focus should be on experimental and mechanistic studies. It is at present unclear when science can provide more reliable evidence, given that the ELF magnetic fields debate awaits its breakthrough since several decades. The situation is somewhat different for mobile telephones, as due to the widespread use, risks will ultimately impact incidence rates of diseases. Policy makers and individuals may consider precautionary options, such as using wired hands-free devices when using mobile phones, restricting mobile phone use in children and considering exposure reduction measures when planning the building of new power lines.

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