

Use of mobile phones and cordless phones and the risk for brain tumours – a case-control study

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Aim:

The aim of this new study is to investigate if use of mobile and cordless phones is associated with an increased risk for brain tumours in men and women aged 18-75 years at the time of diagnosis. They are all living in Sweden and were diagnosed during the time period 2007-2009. Especially long term (>10 years) use is studied as well as the risk in different age groups and separately in men and women.

Background:

Use of the wireless technology for communication has increased rapidly both in different occupations and during leisure time during the recent decade. This is especially the situation for use of both mobile phones and cordless phones (DECT). The development has been driven by technological achievements and potential health risks are not well investigated, especially the risk for brain tumours.

The present guideline of 2 W/kg (SAR) for exposure to microwaves from mobile phones is based on heating (thermal effect) by radiofrequency radiation in the range of 400-2100 MHz. A number of studies show, however, non-thermal effects (not due to heating) from microwave radiation, for example on the blood-brain barrier (Salford et al 2003, Töre et al 2001, Nittby 2008), changes of the protein configuration and heat shock protein (de Pomerai et al 2000, French et al 2000, Kwee et al 2001, Leszczynski et al 2002), and production of micronuclei in lymphocytes (Garaj-Vrhovac et al 1992, Zotti-Martelli et al 2000, Tice et al 2002). The experimental REFLEX-study showed biological effects from radiofrequency radiation of 0.3 W/kg, that is below current guideline of 2 W/kg (REFLEX 2004). A summary of non-thermal biological effects can be found in different publications (Belyaev 2005, Sage, Carpenter 2007, Hardell, Sage 2008). An increased glucose metabolism in parts of the brain (frontal and parietal lobes) exposed to radiofrequency radiation was recently published, and this could not be explained by a heating effect (Volkow et al 2001), as also discussed in an editorial (Lai, Hardell 2011).

The Nordic countries were among the first to start the use of mobile phones. The analogue phone (NMT 450) was introduced in 1981. First it was mostly used in cars with an external antenna but portable analogue phones were used since 1984. The NMT 450 system was closed down December 31, 2007. NMT 900 was used during 1986 to 2000. The digital system, GSM 900/1800 MHz was started in 1991 and is the most common mobile phone type in Sweden since late 1990's. The third generation, 3G, of mobile phones operating in the range of 1900 to 2100 MHz was introduced in 2003 in Sweden. Now the fourth generation, 4G, is available on the market.

Cordless desktop phones have been used in Sweden since 1988. First the analogue system using the frequency range 800-900 MHz was used. Since the beginning of the 1990's the digital system, DECT phone, operating at 1900 MHz frequency is used. Exposure to

radiofrequency radiation from a DECT phone is in the same order of magnitude as from the GSM mobile phone (Redmayne et al 2010).

In two large case-control studies, the largest from a single research unit, we have found a statistically significantly increased risk for glioma (malignant brain tumour) and acoustic neuroma (a tumour of the hearing nerve) for use of mobile phones and cordless phones (Hardell et al 2006a, 2006b). The risk was largest for long term use, more than 10 years. For acoustic neuroma an increased risk was also found for more short time use, recently also shown in a study from Japan (Sato et al 2011). Regarding meningioma, the most common benign brain tumour, we did not find an increased risk. We have also studied use of wireless phones and the risk for other tumours, such of the salivary gland, testicular cancer and lymphoma (non-Hodgkin lymphoma). We found an association with the skin type of non-Hodgkin lymphoma but no clear associations with other tumour types. We have summarized results of all our studies previously (Hardell et al 2009).

We have performed more analyses of our study encompassing the time period 1997-2003, as well as regarding the incidence of brain tumours (Hardell, Carlberg 2009, Hardell et al 2011). The yearly age standardized incidence of astrocytoma increased during 2000-2007 among persons aged more than 19 years. This was seen in spite of the deficient reporting to the Swedish Cancer Registry (Barlow et al 2009). Of interest is that we saw the highest risk for astrocytoma and acoustic neuroma in persons who had used mobile phone or cordless desktop phone before the age of 20 years. In a separate study on patients who had died in glioma we found an increased risk for use of mobile phone (Hardell et al 2010a). As control subjects persons who had died in other diseases were used. Relatives were interviewed in both groups, that is exposure information was obtained in the same way for cases and controls in the study.

A number of studies have been used by WHO, the Interphone studies, and the results have been published for glioma and meningioma. Cumulative use of a mobile phone for 1640 hours or more yielded a statistically significant increased risk for glioma, odds ratio = 1.40, 95% confidence interval = 1.03-1.89. If the mobile phone had been used on the same side of the head as the tumour was located the risk increased further to 1.96, 95% confidence interval 1.22-3.16, that is exposure in the area of the brain with highest exposure to microwaves from the mobile phone. Furthermore, the risk was highest in the temporal lobe, which is the area of the brain closest to the mobile phone during calls. Interestingly when we reanalysed our data using the same criteria as used in the Interphone studies (same age group, use of DECT included among the 'unexposed', same groups of cumulative use and latency period). The results were thereby similar as in the Interphone publication (Hardell et al 2010b). The Interphone findings have been commented further by two of the authors, Cardis and Sadetzki (2011).

In our previous studies we did not find a consistent pattern of increased risk for meningioma. These results are similar as in the Interphone publication. We have reported a statistically significant increased risk for acoustic neuroma. These results have not yet been published from the Interphone group although the studies ended in 2004.

Work procedure:

Cases: The study includes the whole Swedish country. The cases were diagnosed with a brain tumour between 2007 - 2009 (Gothenburg region 2008 - 2009). They were all alive and both benign and malignant brain tumours were included with the ICD (International Code of Diseases) code = 193.0. Both men and women aged 18 – 75 years were included. All new

cases that were reported to the Swedish Cancer Registry were notified to us. The responsible treating physician of the respective patient was contacted for permission to include the patient in the study.

Controls: One person was identified from the Swedish Population Registry and was used as a control subject to each case. They were matched on gender and age.

Exposure: All cases and controls received a questionnaire by post. If the questionnaire was not answered in detail a supplementary telephone interview was made by a trained interviewer. Questions were asked on use of mobile and cordless phones. The year for first use was assessed as well as average number of minutes of use in a day, the ear that had mostly been used (or equally much both ears), use in a car with external antenna, hands free use, number of mobile phones used over the years etc. Also other questions were asked on e.g. lifetime occupations, exposure to chemicals, ionizing radiation, x-rays, smoking habits etc.

All questionnaires received a unique id-number that did not show if it is a case or a control. Type of tumour is obtained from the cancer registry and histopathology reports. Copies of computer tomography (CT) or MRI of the brain are asked for each case in order to assign an anatomical localisation of the brain tumour.

Statistical analysis: Unconditional logistic regression analysis will be performed for calculation of the risk; odds ratio and 95% confidence interval. Adjustment will be made for age, gender, year of diagnosis and socioeconomic index. Use of mobile and/or cordless phone will be compared with no use. Special analysis will be performed for cumulative use over the whole time period, number of years for use and age at first use of a wireless phone. Different types of brain tumours such as glioma, acoustic neuroma and meningioma will be analysed separately. Also other exposures will be analysed. The size of the study gives 80 % probability to find a risk of 1.3 at the 95% significance level.

Gender: Both male and female cases are included in the study. Glioma is somewhat more common in men, whereas meningioma is more common in women. These differences will be analysed in more detail. In the German part of the Interphone studies use of mobile phones yielded a somewhat higher risk for glioma in women than in men (Schüz et al 2006). This will be further analysed.

Current status of the study:

Reported from the Cancer Registry	2571 patients
Deceased before interview	551 patients
Excluded wrong diagnosis, no address	213 patients
Too ill to participate	67 patients
No to include from treating physician	85 patients
Yes to include from treating physician	1655 patients

Posted questionnaire	Cases	Controls
Total	1655	1655
Returned	1459 (88%)	1414 (85%)
Refused to participate	196	241

All questionnaires from cases and controls that participate in the study have been returned. Also all supplementary phone interviews have been performed. The questionnaire consists of

11 pages. The first page includes the working history with type of work and years for the specific job. All occupations shall be coded according to the Nordic code for classification (NYK) and socioeconomic index for the different jobs.

Different exposures are assessed in groups of 32 questions. Each question is subdivided into other questions so that more than 100 will be coded for the statistical analysis. These questions include among other items use of computers, wireless communication (WLAN), work with exposure to electromagnetic fields, ionizing radiation, x-rays, solvents, herbicides, other agents, hereditary questions, living close to municipal incinerators, radio/TV masts, base stations, smoking habits etc. Special questions deal with use of mobile and/or cordless phones. All exposures shall be quantified with number of days for cumulative use, years for use, type of for example chemicals etc. Regarding wireless phones, the type of phone is coded as is total years of use, cumulative hours of use, ear mostly used for calls etc.

Copies of CT and MRI scans for all cases will be asked for from the different radiology departments in Sweden. Histopathology reports are obtained for all cases with unclear type of brain tumour. This is performed after permission from the patient.

Based on our previous studies this part of the study includes at average 20 minutes for coding and 10 minutes for registration in a database of each questionnaire. This part of the study involves in total about 1400 hours of work or 9 months in total.

Scrutinizing the data to correct any obvious typing errors follows this part. After that statistical analysis will be performed, in total 4 months of statistical work including quality work on the data base.

A number of publications are planned:

1. The risk for glioma and use of wireless phones.
2. The risk for meningioma and use of wireless phones.
3. The risk for acoustic neuroma and use of wireless phones.
4. The risk for glioma, occupation and other exposures.
5. The risk for meningioma, occupation and other exposures.
6. The risk for acoustic neuroma, occupation and other exposures.
7. Special aspects on use of mobile and cordless phones and the risk for brain tumours.

Significance of the study:

It is extremely important to further study the risk for brain tumours associated with use of both mobile and cordless phones. This is a large study from one research group. It will give information on different types of brain tumours and long-term use of wireless phones and also the risk in different age groups. A number of other exposures are also studied including the potential interaction between exposure to radiofrequency radiation and other factors.

Budget for the remaining part of the study:

Research secretary 9 months, 3 790 Euro/month = 34 110 Euro

Statistician 4 months, 4194 Euro/month = 16 776 Euro

Total = 50 886 Euro (including social fees)

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