

Mobile phone use and risk of glioma in adults: case-control study

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Abstract

Objective To investigate the risk of glioma in adults in relation to mobile phone use.

Design Population based case-control study with collection of personal interview data.

Setting Five areas of the United Kingdom.

Participants 966 people aged 18 to 69 years diagnosed with a glioma from 1 December 2000 to 29 February 2004 and 1716 controls randomly selected from general practitioner lists.

Main outcome measures Odds ratios for risk of glioma in relation to mobile phone use.

Results The overall odds ratio for regular phone use was 0.94 (95% confidence interval 0.78 to 1.13).

There was no relation for risk of glioma and time since first use, lifetime years of use, and cumulative number of calls and hours of use. A significant excess risk for reported phone use ipsilateral to the tumour (1.24, 1.02 to 1.52) was paralleled by a significant reduction in risk (0.75, 0.61 to 0.93) for contralateral use.

Conclusions Use of a mobile phone, either in the short or medium term, is not associated with an increased risk of glioma. This is consistent with most but not all published studies. The complementary positive and negative risks associated with ipsilateral and contralateral use of the phone in relation to the side of the tumour might be due to recall bias.

Introduction

Gliomas are the most common malignancy of the central nervous system in adults.¹ It is still unclear whether the use of mobile phones is associated with an increased risk of gliomas and other brain tumours, and little is known about potential mechanisms.² Most published epidemiological studies on mobile phone use and gliomas have not generally reported any increased risk either overall or with long term use.³⁻⁶ Individual studies have found positive associations between high grade astrocytoma (glioma) and phone use ipsilateral to the side of the tumour,⁷ brain tumours and phone use in rural areas,⁸ and use of analogue mobile phones.^{7,9}

We carried out a large population based case-control study of 966 patients with glioma in the United Kingdom. This study is part of the Interphone project,¹⁰ an international collaboration of 13 countries investigating mobile phone use and the risk of intracranial tumours.

Methods and participants

The study took place in five areas: Thames regions in south east England, Trent, West Midlands, West Yorkshire, and southern Scotland. The total catchment

population (28.4 million) comprised 48.3% of the UK population. Cases were ascertained from multiple sources, including hospital departments and cancer registries (see bmj.com for details). Data on site, laterality (left, right, central), and grade of tumour (WHO grade high III-IV; low I-II¹¹) were abstracted from scan and pathology reports.

Controls were randomly selected from general practitioners' lists by a preset algorithm (see bmj.com for details). With the participant's informed consent, trained interviewers conducted a computer assisted personal interview. For 69 patients with glioma (7%), interviewers conducted proxy interviews, mainly with spouses.

When participants reported that they had ever made one or more calls each week on average for a period of six months or longer, they were asked a detailed set of questions on mobile phone use. For each phone, the interviewer recorded the network operator, start and stop year, and the number and duration of calls made and received. Additional details were gathered on which side of the head the phone was mostly used (50% or more of the time) and factors influencing emitted power levels to the head, including use of hands-free kits and whether the phone was used mainly in an urban or rural area or equally in both.¹²

In the analysis, we defined regular phone use as use for at least six months in the period more than a year before diagnosis. The exposure period for people with glioma was calculated up to a year before the date of diagnosis. An equivalent reference date was required for control participants that allowed for the increase in mobile phone use over the study period. As controls tended to be interviewed after the patients with glioma, exposure indices were calculated up to a year before this reference date for controls (that is, a one year latency time was used). Additional analyses were carried out with a five year latency time.

Statistical analysis

For statistical analysis we used unconditional logistic regression adjusted for nine regions (five regions within the south east and the four northern regions), age at reference date (five year categories), sex, deprivation (Townsend score¹³), and combinations of interview year and lag time to account for the fact that controls were, on average, interviewed later in the study period than patients with glioma. We derived odds ratios for cumulative use, and separately for high and low grade tumours and urban versus rural use. We assessed the risk of a tumour ipsilateral or contralateral to side of phone use (see bmj.com).

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Results

Researchers interviewed 966 cases (367 in the south east and 599 in northern areas) and 1716 controls (630 and 1086). The main reasons for non-participation were the participant was too ill or had died before interview (cases 30%, controls <1%), non-response (cases 2%, controls 21%), refusal (cases 10%, controls 29%), and other reasons (see bmj.com) (cases 7%, controls 5%). Overall response rates were 51% for patients with glioma and 45% for controls. Interviewed patients with glioma were broadly representative of the overall set of those eligible by age and sex but differed by deprivation category, being significantly more affluent (χ^2 test for trend, $P < 0.001$).

Table 1 shows the demographic distribution of interviewed cases and controls. The proportion of men was higher among the patients with glioma than in the control group.

We found an odds ratio of 0.94 (95% confidence interval 0.78 to 1.13) for glioma for regular phone users compared with those who never or only occasionally used mobile phones (see bmj.com). There was no association of risk with lifetime years of use, cumulative hours of use, cumulative numbers of calls, nor cumulative hours of use over 10 years before the reference date (table 2).

We found a significant odds ratio of 1.24 (1.02 to 1.52) for a tumour ipsilateral to side of phone use and a reduced odds ratio for contralateral use (0.75, 0.61 to 0.93) (see bmj.com). Similar respective excesses and deficits were present for all exposure measures of mobile phone use, including use for ≥ 10 years (ipsilateral 1.60, 0.92 to 2.76; contralateral 0.78, 0.43 to 1.41). To investigate this further, we analysed regular use ipsilateral and contralateral to handedness, which gave odds ratios of 0.78 (0.62 to 0.99) and 1.07 (0.85 to 1.35), respectively. The concordance between reported side of use and handedness was 59% for cases and 64% among controls. The method of Inskip et al³ gave an

Table 1 Demographic distributions in cases and controls. Figures are numbers (percentages) of participants

	Cases (n=966)	Controls (n=1716)
Region:		
Thames regions	367 (38.0)	630 (36.7)
Southern Scotland	152 (15.7)	277 (16.1)
Trent	199 (20.6)	372 (21.7)
West Midlands	115 (11.9)	207 (12.1)
West Yorkshire	133 (13.8)	230 (13.4)
Age at reference date (years):		
18-29	100 (10.4)	112 (6.5)
30-39	199 (20.6)	281 (16.4)
40-49	216 (22.4)	429 (25.0)
50-59	328 (34.0)	645 (37.6)
60-69†	123 (12.7)	249 (14.5)
Men	604 (62.5)	829 (48.3)
Women	362 (37.5)	887 (51.7)
Deprivation score*:		
1 (most affluent)	257 (26.6)	513 (29.9)
2	229 (23.7)	386 (22.5)
3	178 (18.4)	334 (19.5)
4	181 (18.7)	292 (17.0)
5 (least affluent)	121 (12.5)	191 (11.1)

*Townsend score (area based measure of deprivation) categorised into five equally sized groups based on 2001 census data.
†Control group includes seven people aged >69 at reference date.

Table 2 Odds ratios and 95% confidence intervals for risk of glioma in relation to mobile phone exposure.* Figures are numbers (percentages) of participants

Factor and level of exposure	Cases (n=966)	Controls (n=1716)	Odds ratio† (95% CI)
Frequency of use:			
Never/non-regular	456 (47.2)	818 (47.7)	1.00
Regular	508 (52.6)	898 (52.3)	0.94 (0.78 to 1.13)
Not known	2 (0.2)	0	—
Years since first use:			
Never/non-regular	456 (47.2)	818 (47.7)	1.00
1.5-4‡	271 (28.1)	515 (30.0)	0.90 (0.73 to 1.11)
5-9	170 (17.6)	270 (15.7)	1.04 (0.80 to 1.34)
≥ 10	66 (6.8)	112 (6.5)	0.90 (0.63 to 1.28)
Not known	3 (0.3)	1 (0.1)	—
Lifetime years of use:			
Never/non-regular	456 (47.2)	818 (47.7)	1.00
0.5-4	342 (35.4)	623 (36.3)	0.93 (0.76 to 1.14)
5-9	115 (11.9)	206 (12.0)	0.88 (0.66 to 1.17)
≥ 10	48 (5.0)	67 (3.9)	1.14 (0.74 to 1.73)
Not known	5 (0.5)	2 (0.1)	—
Cumulative hours of use§:			
Never/non-regular	456 (47.2)	818 (47.7)	1.00
≤ 99	225 (23.3)	444 (25.9)	0.94 (0.76 to 1.17)
99- ≤ 544	128 (13.3)	218 (12.7)	0.87 (0.65 to 1.15)
> 544	135 (14.0)	217 (12.6)	0.94 (0.71 to 1.23)
Not known	22 (2.3)	19 (1.1)	—
Cumulative number of calls§:			
Never/non-regular	456 (47.2)	818 (47.7)	1.00
≤ 2071	237 (24.7)	444 (25.9)	0.99 (0.80 to 1.23)
2071- ≤ 6909	102 (10.6)	217 (12.6)	0.70 (0.52 to 0.93)
> 6909	146 (15.1)	218 (12.7)	0.97 (0.74 to 1.28)
Not known	25 (2.6)	19 (1.1)	—
Cumulative hours of use ≥ 10 years ago¶:			
Never/non-regular	456 (47.2)	818 (47.7)	1.00
< 10 years	429 (44.4)	772 (45.0)	0.93 (0.77 to 1.13)
≥ 10 years, ≤ 113 hours	23 (2.4)	56 (3.3)	0.61 (0.36 to 1.04)
≥ 10 years, > 113 hours	39 (4.0)	54 (3.2)	1.11 (0.70 to 1.75)
Not known	19 (2.0)	16 (1.0)	—
Proportion urban/rural at first use:			
Never/non-regular	456 (47.2)	818 (47.7)	1.00
Mainly urban	241 (24.9)	471 (27.4)	0.83 (0.66 to 1.03)
Mainly rural	49 (5.1)	84 (4.9)	0.98 (0.66 to 1.46)
Both	215 (22.3)	343 (20.0)	1.05 (0.83 to 1.31)
Not known	5 (0.5)	0	—
According to tumour grade**			
Frequency of use in those with high grade tumours:			
Never/non-regular	331 (50.9)	818 (47.7)	1.00
Regular	317 (48.8)	898 (52.3)	0.95 (0.77 to 1.17)
Not known	2 (0.3)	0	—
Frequency of use in those with low grade tumours:			
Never/non-regular	122 (39.9)	818 (47.7)	1.00
Regular	184 (60.1)	898 (52.3)	0.85 (0.63 to 1.13)
Not known	0	0	—
According to side of phone use††			
Frequency of ipsilateral use*:			
Never/non-regular	550 (66.3)	1230 (71.7)	1.00
Regular	278 (33.5)	486 (28.3)	1.24 (1.02 to 1.52)
Not known	2 (0.2)	0	—
Frequency of contralateral use*:			
Never/non-regular	629 (75.8)	1225 (71.4)	1.00
Regular	199 (24.0)	491 (28.6)	0.75 (0.61 to 0.93)
Not known	2 (0.2)	0	—

*Reference category is never or non-regular use of any type of mobile phone and, in ipsilateral analysis, phone use only on opposite side of tumour, and in contralateral analysis, phone use only on same side as tumour.
†Odds ratios adjusted for age at reference date (in 5 year age groups), sex, region, Townsend deprivation category, and interview reference date category.
‡Lower limit 1.5 years ago because regular phone use defined as phone use of at least six months' duration at least one year before reference date.
§For cumulative number and duration of calls category cut-off points were median and 75th centile of use for controls who were regular phone users.
¶Use over 10 years before reference date for controls and diagnosis date for cases.
**10 tumours (1.7%) were of undetermined grade.
††In 449 (46.5%) cases tumour was classified as being on right side of head and in 387 (40.1%) on left side, 49 cases (5.1%) were excluded from this analysis because tumour was central, 81 cases (8.4%) because side of tumour was unknown, six others where side of phone use was unknown were also excluded.

overall relative risk of 1.3 (Fisher's exact $P < 0.001$) for a tumour ipsilateral to the side of phone use.

Use of analogue phones did not increase the risk of developing glioma (see bmj.com).

Discussion

In this large study on associations between use of mobile phone and the risk of developing a glioma in a UK population we did not find a raised risk associated with phone use.

Analogue phones emit higher average power levels than digital phones.¹⁴ If mobile phone use was causally linked to the development of glioma and risk was related to power level, we would predict a higher risk for analogue phone use than for digital phones. As in some^{5 6 15} but not all^{7 9} previous reports we found no association between risk of glioma and use of analogue phones overall or with time since first use, lifetime years of use, or cumulative hours or number of calls.

In Sweden Hardell et al reported raised risks for mobile phone use ipsilateral to the side of development of high grade astrocytomas (the principal subtype of glioma)⁷ and for rural use in different analyses of the same study.⁸ Several other studies, however, could not confirm these results and the methods were criticised.¹⁶⁻¹⁸ Our laterality analyses showed a significantly raised risk for ipsilateral phone use and a significantly reduced risk for contralateral use. These "complementary risks" above and below unity, which we observed for all measures of mobile phone use, can probably be explained by recall bias.¹⁸ Generally, individuals are likely to overestimate their actual use of mobile phones,¹⁹ and this may have exaggerated the effect of differential reporting for laterality.

Potential bias

Case-control studies are subject to certain biases and particularly participation bias.²⁰ We interviewed 51% of those patients with glioma who were eligible, mainly because rapid death prevented us approaching all of them. As early death is most likely in patients with high grade tumours, it is not surprising that participation rates were higher in those with low grade tumours. A bias in these results would occur only if mobile phone use was related to severity of tumour, which was not supported by our analysis, where odds ratios for mobile phone use showed no increased risk for high or low grade tumours.

There is also potential for the introduction of participation bias into the control group. All controls were selected to represent the general population by using the sampling frame of general practitioners' lists. The overall response rate for controls was relatively low (45%) compared with previously published studies from the Nordic countries^{5 6} on mobile phone use and risk of glioma. The principal reason for non-participation of controls was that they were "uncontactable," and constraints imposed by ethical approval bodies prevented more than one follow-up attempt. Our interviewed controls were more affluent than their non-interviewed counterparts and the interviewed patients with glioma. Though we adjusted for deprivation in all the analyses, this cannot completely remove its potential influence.

What is already known on this topic

Gliomas are a specific type of brain tumour for which the causes are generally unknown, but concern has been expressed over a possible link with using a mobile phone

What this study adds

This large case-control study found no increased risk of developing a glioma associated with mobile phone use either in the short or medium term

There is generally a lack of convincing and consistent evidence of any effect of exposure to radio-frequency field on risk of cancer.^{21 22} Overall our findings are consistent with this and with most studies on mobile phone use. The positive association found between risk of glioma and ipsilateral mobile phone use was accompanied by a negative association for the opposite side of use to the tumour. Although it is possible the ipsilateral association represents a real effect, this finding is probably explained by recall bias, with patients with glioma systematically over-reporting use on the same side as their tumour and consequently under-reporting use on the opposite side. This study suggests that there are no substantially raised risks of glioma in the 10 years after first mobile phone use. Only future studies will be able to address longer latency periods for the development of glioma.

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Competing interests: The University of Leeds has received some financial support on behalf of the four centres of the UK northern study from the UK network operators (O2, Orange, T-Mobile, Vodafone, 3) under legal signed contractual agreements which ensure complete independence for the scientific investigators. While employed at the University of Birmingham MJAvT received funding from O2, Orange, T-Mobile, and Vodafone to carry out a feasibility study of health effects from radiofrequency exposure among employees of broadcasting and telecommunication industries.

Ethical approval: Multicentre research ethics committees for the south east and Scotland and all relevant local research ethics committees.

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Are some people sensitive to mobile phone signals? Within participants double blind randomised provocation study

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Abstract

Objective To test whether people who report being sensitive to mobile phone signals have more symptoms when exposed to a pulsing mobile signal than when exposed to a sham signal or a non-pulsing signal.

Design Double blind, randomised, within participants provocation study.

Setting Dedicated suite of offices at King's College London, between September 2003 and June 2005.

Participants 60 "sensitive" people who reported often getting headache-like symptoms within 20 minutes of using a global system for mobile communication (GSM) mobile phone and 60 "control" participants who did not report any such symptoms.

Intervention Participants were exposed to three conditions: a 900 MHz GSM mobile phone signal, a non-pulsing carrier wave signal, and a sham condition with no signal present. Each exposure lasted for 50 minutes.

Main outcome measures The principal outcome measure was headache severity assessed with a 0-100 visual analogue scale. Other outcomes included six other subjective symptoms and participants' ability to judge whether a signal was present.

Results Headache severity increased during exposure and decreased immediately afterwards. However, no strong evidence was found of any difference between the conditions in terms of symptom severity. Nor did evidence of any differential effect of condition between the two groups exist. The proportion of sensitive participants who believed a signal was present during GSM exposure (60%) was similar to the proportion who believed one was present during sham exposure (63%).

Conclusions No evidence was found to indicate that people with self reported sensitivity to mobile phone signals are able to detect such signals or that they react to them with increased symptom severity. As sham exposure was sufficient to trigger severe symptoms in some participants, psychological factors may have an important role in causing this condition. **Trial registration** ISRCTN81432775.

Introduction

The health effects most often attributed to mobile phone use are non-specific symptoms, the most commonly reported of which are headache, burning, dizziness, fatigue, and tingling.¹ Mechanisms to explain these phenomena remain speculative, and although the pulsing nature of "global system for mobile communication" (GSM) signals has been suggested to be partly to blame,² experiments that have exposed healthy adults to GSM signals under blind conditions have not found any effect on the reporting of symptoms.³

Of particular interest are people who report symptoms almost every time they use a mobile phone.⁴ This phenomenon falls within the broader category of "electromagnetic sensitivity," a medically unexplained condition in which non-specific symptoms are reported after perceived exposure to electrical devices, including mobile phones, visual display units, and power lines. Provocation studies that have exposed people who report electromagnetic sensitivity to electromagnetic fields under blind conditions have so far failed to provide any good evidence linking the

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