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Long-Term Mobile Phone Use and Brain Tumor Risk

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Handheld mobile phones were introduced in Sweden during the late 1980s. The purpose of this population-based, case-control study was to test the hypothesis that long-term mobile phone use increases the risk of brain tumors. The authors identified all cases aged 20–69 years who were diagnosed with glioma or meningioma during 2000–2002 in certain parts of Sweden. Randomly selected controls were stratified on age, gender, and residential area. Detailed information about mobile phone use was collected from 371 (74%) glioma and 273 (85%) meningioma cases and 674 (71%) controls. For regular mobile phone use, the odds ratio was 0.8 (95% confidence interval: 0.6, 1.0) for glioma and 0.7 (95% confidence interval: 0.5, 0.9) for meningioma. Similar results were found for more than 10 years' duration of mobile phone use. No risk increase was found for ipsilateral phone use for tumors located in the temporal and parietal lobes. Furthermore, the odds ratio did not increase, regardless of tumor histology, type of phone, and amount of use. This study includes a large number of long-term mobile phone users, and the authors conclude that the data do not support the hypothesis that mobile phone use is related to an increased risk of glioma or meningioma.

case-control studies; cellular phone; glioma; meningioma

Abbreviations: CI, confidence interval; DECT, digital enhanced cordless telecommunications; UICC, International Union against Cancer.

Human exposure to radiofrequency radiation has increased dramatically during recent years from widespread use of mobile phones. If radiofrequency radiation has a carcinogenic effect, the exposure poses an important public health problem, and intracranial tumors would be of primary interest. A biologic mechanism that could explain any possible carcinogenic effect from radiofrequency radiation has not been identified. It is generally agreed that the heating of tissue by radiofrequency radiation from mobile phone use is negligible and that any carcinogenic effect would have to be mediated through a nonthermal mechanism. The results of most previous studies of brain tumors in mobile phone users have been negative (1, 2), although a Finnish study and a Swedish study have indicated an increased risk (3, 4). Studies of ionizing radiation (5) have indicated that the induction period of radiation-induced solid tumors is probably at least 10 years. If, however, the mechanism is one of promotion rather than initiation, a shorter induction period would be possible. No studies to date have had an exposure time long enough to properly address the potential adverse late health effects of mobile phone use.

Handheld mobile phones were introduced in Sweden during the late 1980s and were in common use relatively early. This makes the Swedish population suitable for a study aiming at testing the hypothesis that long-term mobile phone use increases the risk of brain tumors. The specific aim of this study was to investigate the association between mobile phone use and the risk of glioma and meningioma, the two most common types of intracranial tumors. The Swedish study of brain tumors reported here is part of the INTERPHONE Study (6). We have previously reported results for acoustic neuroma (7).

MATERIALS AND METHODS

The study population in this case-control study included approximately 3.7 million people and was restricted to all residents aged 20–69 years in the geographic areas covered

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by the regional cancer registries in Umeå, Stockholm, Göteborg, and Lund. The study period was from September 1, 2000, to August 31, 2002. The ethics committees at Karolinska Institutet and the universities of Umeå, Göteborg, and Lund approved the study.

Case ascertainment

Eligible cases were all individuals diagnosed during the study period with intracranial glioma (*International Classification of Diseases*, Tenth Revision, code C71; *International Classification of Diseases for Oncology*, Second Edition, codes 9380–9384, 9390–9394, 9400–9401, 9410–9411, 9420–9424, 9430, 9440–9443, 9450–9451, 9460, 9480–9481, and 9505) or meningioma (*International Classification of Diseases*, Tenth Revision, code C70; *International Classification of Diseases for Oncology*, Second Edition, codes 9530–9539). Cases were identified continuously during the study period at the neurosurgery, oncology, and neurology clinics at all hospitals within the study area. Trained nurses or a psychologist visited the clinics every week to ensure a rapid ascertainment of cases. The regional cancer registries were searched approximately every third month for additional case identification, to make sure that no cases had been missed. We identified in total 499 glioma cases and 320 meningioma cases. Four percent ($n = 20$) of the glioma cases and 9 percent ($n = 28$) of the meningioma cases were identified from the cancer registry.

Medical records for all cases were examined to confirm the diagnosis, to establish the date of diagnosis (defined as the date of the first medical examination leading to the diagnosis, usually when the first radiograph was taken), and to determine the location of the tumor. The date of diagnosis was used as the reference date in the exposure assessment.

Control selection

Controls were randomly selected from the study population stratified on age (in 5-year groups), gender, and residential area. The control selection was made from the continuously updated registry of the Swedish population approximately every second month during the study period. Controls were selected to cover the required number per case stipulated by the common core protocol for the INTERPHONE Study (one per brain tumor case, two per acoustic neuroma case, and three per parotid gland tumor case). As we did not use a matched control selection, the entire set of controls was used for all studied outcomes. In total, 956 controls were identified. The ''referent date'' for controls was defined as the date of identification of the control, adjusted for the average time difference between the date of identification and the date of diagnosis of the cases. Referent dates for controls were adjusted separately for glioma and meningioma cases, because the average time between diagnosis and identification was shorter for glioma cases.

Data collection

All interviews and contacts with cases and controls were made by nurses and one psychologist employed for this purpose. Before the data collection, an interviewer-training workshop was held in Copenhagen, Denmark, for interviewers in all the Scandinavian centers participating in the INTERPHONE Study, according to the protocol of the international study to ensure uniform data collection procedures. Regular refresher meetings were held nationally.

All cases and controls were approached as soon as possible after identification. Cases were contacted after permission from the treating physician or the head of the clinic. For both cases and controls, we excluded persons who were completely deaf (no cases and one control) prior to the referent date or who did not possess the intellectual and linguistic skills necessary to complete an interview (23 cases and 26 controls), as judged by the nurses or the psychologist.

Information about mobile phone use and other possible risk factors, such as family history of cancer and ionization radiation, was collected through personal interviews using a computer program that guided the interview with questions read by the interviewer from a laptop computer screen. The responses were entered directly into the computer by the interviewer. All interviewers were provided with cards displaying photographs of mobile phones with information about make, model, and year of introduction. An interview lasted approximately 45 minutes. Interviews with glioma and meningioma cases took on average 2–3 minutes longer than interviews with control participants. Directly after all personal interviews, the interviewer made an assessment of the quality of the interview on a five-grade scale. Persons that were unable to participate in a personal interview would offered a telephone interview instead. Those who refused participation in any kind of interview were asked if they would answer a paper questionnaire. If a person still refused, we asked if he/she could answer three short questions over the phone. The purpose of the three questions was to evaluate potential selection bias due to nonparticipation. If a case had died, the closest relative was contacted as a proxy respondent. More details about data collection and exposure assessment have been described previously (7).

Classification of exposure

Regular mobile phone use was defined as use of a mobile phone on average once per week during at least 6 months. Exposure within 1 year of the referent date was not considered. We defined as unexposed those subjects who reported that they had never or only rarely (not regularly) used a mobile phone. We calculated cumulative mobile phone use, categorized into less than 30 hours, 30–499 hours, and 500 hours or more (cutpoints approximately at the 25th and 75th percentiles for controls). The cumulative number of mobile phone calls was calculated and categorized into less than 650 calls, 650–8,449 calls, and 8,550 calls or more (cutpoints at approximately the 25th and 75th percentiles for controls). The number of years of regular use was categorized into less than 5 years, 5–9 years, and 10 years or more. Time since first regular use was categorized into less than 5 years, 5–9 years, and 10 years or more. Usages of analog (Nordic Mobile Telephone (NMT), continuous-signal) and digital (Global System Mobile (GSM), varying-radiofrequency)

mobile phones were also analyzed separately. Sensitivity analyses were performed defining as unexposed only those who had never used a mobile phone.

Usage of hands-free devices reduces the exposure from radiofrequency radiation to the head by more than 90 percent (8). In an analysis of the cumulative hours of mobile phone use, the participants who reported almost always using a hands-free device were considered as unexposed. For participants reporting use of a hands-free device more than half of the time, 75 percent of the time used for calling was excluded; for usage half of the time, 50 percent of the time was excluded; and for usage less than half of the time, 25 percent of the time was excluded.

Separate analyses were performed for mobile phone use in urban and rural areas because the radiofrequency radiation exposure from a mobile phone is directly related to the output power level used by the phone to communicate with the base station. There are indications of higher power levels in rural than in urban areas (9).

In the analyses, glioma was also stratified according to grade and histopathologic subtype, where low-grade glioma was categorized as World Health Organization grade I–II and high-grade glioma was categorized as World Health Organization grade III–IV. The histopathologic subtype glioblastoma was analyzed separately. In addition, for both glioma and meningioma, analyses were performed stratified on tumor localization. Tumors partly or totally located in the parietal and temporal lobes were categorized into one subgroup that was considered to have the highest exposure from the mobile phone (10, 11). Tumors in the frontal lobe were treated as one subgroup, and tumors located elsewhere were treated as a third group.

If radiofrequency exposure from mobile phone use has an effect on brain tumor risk, one would expect the highest risk for those places that receive the highest exposure, that is, the side of the head where the phone is usually held. To analyze the possible association between laterality of phone use and laterality of tumors, we studied left- and right-side tumors separately. The cases were divided into left-side and right-side groups, depending on the localization of the tumor. The controls were randomly (within strata of stratification variables) assigned to two separate control groups: one for cases with left-side tumors and one for cases with right-side tumors. For both cases and controls, exposure was defined as ipsilateral phone use or use of the phone on both sides, whereas contralateral use was considered unexposed. Based on this, side-specific odds ratios were calculated and then pooled into one odds ratio. In addition, laterality analyses were made with restriction to tumors in the temporal and parietal lobes. To test for potential recall bias, we made similar analyses where contralateral phone use or use on both sides was considered exposed, and ipsilateral use was considered unexposed. Results showing no overall risk increase but an increased risk for ipsilateral phone use and a decreased risk (protective effect) for contralateral use would be taken as an indication of recall bias, that is, a tendency among cases to overreport use of the phone on the same side as the tumor is located.

In addition to our analysis of mobile phones, we analyzed if the use of European digital enhanced cordless telecommunications (DECT) phones increases the risk of glioma or meningioma. Regular DECT phone use was defined with the same criteria as for mobile phone use.

Statistical analysis

Associations between indicators of mobile phone use and the tumors were shown as odds ratios, using unconditional logistic regression models (12), with 95 percent confidence intervals. Adjustments for the stratification variables (age, gender, residential area) and education (compulsory school, vocational or secondary school, upper secondary school, university) were made in all analyses. Analyses were also performed to investigate possible confounding from a family history of cancer or exposure from ionization radiation during medical examinations or treatment.

RESULTS

Participation rates were 74 percent ($n = 371$) for glioma cases, 85 percent ($n = 273$) for meningioma cases, and 71 percent ($n = 674$) for controls (table 1). Exposure information was collected through face-to-face interviews for the majority of cases and controls (70 percent of all identified gliomas, 81 percent of meningiomas, and 62 percent of controls). Telephone interviews were performed with 4 percent of glioma cases, 4 percent of meningioma cases, and 4 percent of controls, whereas less than 1 percent of cases (for glioma and meningioma together) and 4 percent of controls answered a mailed questionnaire. Proxy respondents were interviewed for 9 percent ($n = 33$) of participating glioma cases and 3 percent ($n = 8$) of meningioma cases. The median time between the date when the case received a confirmed diagnosis and the date of interview was 56 days for gliomas and 69 days for meningiomas. The median time between the first medical examination leading to the diagnosis (usually when the first radiograph was taken) and the date of interview was 87 days for gliomas and 181 days for meningiomas.

Reasons for nonparticipation included refusal (gliomas: 8 percent; meningiomas: 7 percent; controls: 19 percent), illness (gliomas: 12 percent; meningiomas: 5 percent; controls: 1 percent), and failure to reach the individual (gliomas: 5 percent; meningiomas: 2 percent; controls: 9 percent). From histopathologic reports, 88 percent ($n = 328$) of gliomas and 82 percent ($n = 225$) of meningiomas were histologically verified.

The odds ratios did not differ between men and women, and therefore results are presented only for the genders combined. Results were unchanged when adjustments were made for family history of cancer and ionization radiation, and these variables were therefore not included in the final analyses. Moreover, results were also unchanged if answers through mailed questionnaires were excluded (data not shown).

For regular mobile phone use, regardless of duration, the odds ratio was 0.8 (95 percent confidence interval (CI): 0.6, 1.0) for glioma and 0.7 (95 percent CI: 0.5, 0.9) for meningioma (table 2). The odds ratio did not increase with

TABLE 1. Basic characteristics of participating brain tumor cases and controls, Sweden, 2000–2002

	Glioma cases		Meningioma cases		Controls	
	No.	%	No.	%	No.	%
Interviewed participants	371	74	273	85	674	71
Age (years) at reference date						
20–39	73	20	24	9	133	20
40–59	194	52	168	62	354	53
60–69	104	28	81	29	187	28
Sex						
Female	150	40	194	71	356	53
Male	221	60	79	29	318	47
Education*						
Compulsory school	73	20	53	19	143	21
Vocational/secondary school	104	28	97	36	191	28
Upper secondary school	83	22	32	12	129	19
University	108	29	88	32	203	30
Unknown	3	1	3	1	8	1

* The highest completed education equivalent from the Swedish educational system.

duration of use for any of the tumor types, and the effect was not modified when digital and analog phone users were analyzed separately. All analog phone users had also used a digital phone. The results did not change when the referent category was defined as never use of a mobile phone. Furthermore, excluding interviews with poor quality in the quality assessment did not change the odds ratios (data not shown).

There were no indications of any increased odds ratios for any of the subcategories of glioma (table 3), and there were no indications of any increased odds ratios for any tumor site, regardless of histopathologic subtype (table 4).

The anatomic location could be determined for 94 percent of gliomas and 89 percent of meningiomas. Gliomas were evenly distributed between the right side (43 percent) and the left side (42 percent). Meningioma was somewhat more common on the left side (42 percent) than on the right side (35 percent). Mobile phone use was more common on the right side of the head: 48 percent of gliomas, 50 percent of meningiomas, and 51 percent of the controls reported phone use on the right side. The corresponding numbers for left-side use were 33 percent for gliomas, 37 percent for meningiomas, and 37 percent for the controls. Among controls, 11 percent reported phone use on both sides of the head; for glioma and meningioma cases, the proportion was 13 percent and 10 percent, respectively. Five percent of the gliomas, 3 percent of meningiomas, and less than 1 percent of the controls did not state on which side of the head they generally held the phone. The odds ratios showed overall no association with self-reported laterality of phone use and tumor laterality (table 5). The odds ratio increased among glioma and meningioma cases for ipsilateral mobile phone use during at least 10 years and when phone use started at least 10 years before diagnosis, but these findings were also compatible with no effect. The corresponding results for contralateral mobile phone use showed a decreased odds ratio, also with wide confidence intervals. No increased odds ratios were observed for ipsilateral mobile phone use when the analysis was restricted to the temporal or parietal lobes (table 6).

For participants using mobile phones mainly in rural areas, the odds ratios were 0.8 (95 percent CI: 0.5, 1.3) for glioma and 0.8 (95 percent CI: 0.4, 1.4) for meningioma; for those using the phone mainly in urban areas, the corresponding results were 0.8 (95 percent CI: 0.6, 1.2) for glioma and 0.8 (95 percent CI: 0.5, 1.1) for meningioma. The odds ratio of reported phone use equally in both urban and rural areas was 0.6 (95 percent CI: 0.4, 0.9) for glioma and 0.5 (95 percent CI: 0.3, 0.8) for meningioma. The odds ratio of glioma associated with regular use of DECT phones was 0.8 (95 percent CI: 0.5, 1.1) and of meningioma 0.8 (95 percent CI: 0.5, 1.2).

DISCUSSION

We observed no increased risk of glioma or meningioma related to mobile phone use, regardless of tumor histology, type of phone, and duration of use. Furthermore, we did not observe any increased risk among long-term users in either the analyses among all tumor sites or the analyses restricted to only parietal and temporal tumors on the exposed side. Our results are in agreement with the majority of previous studies (13–16).

This study is population based with a rapid ascertainment of cases through active participation by all clinics involved in the treatment of glioma and meningioma cases. The rapid ascertainment is essential in a study of brain tumors because of the severity of the disease and the relatively short survival time. Control selection randomly from population registries

TABLE 2. Odds ratios* of glioma and meningioma cases according to mobile phone use, Sweden, 2000–2002†

	Glioma cases				Meningioma cases			
	No. of cases	No. of controls	Odds ratio	95% confidence interval	No. of cases	No. of controls	Odds ratio	95% confidence interval
Frequency of use								
Never or rarely‡	157	275	1.0		155	275	1.0	
Regular use§	214	399	0.8	0.6, 1.0	118	399	0.7	0.5, 0.9
Duration of regular use (years)								
<5	120	219	0.9	0.6, 1.2	71	220	0.7	0.5, 1.0
5–9	69	138	0.7	0.5, 1.0	37	138	0.7	0.5, 1.1
≥10	22	33	0.9	0.5, 1.6	8	32	0.7	0.3, 1.6
Time since first regular use (years)								
<5	112	213	0.8	0.6, 1.1	64	213	0.6	0.4, 0.9
5–9	75	139	0.7	0.5, 1.0	40	141	0.7	0.5, 1.1
≥10	25	38	0.9	0.5, 1.5	12	36	0.9	0.4, 1.9
Cumulative use (hours)								
<30	51	105	0.8	0.5, 1.2	30	105	0.6	0.4, 0.9
30–499	98	182	0.8	0.6, 1.1	55	182	0.7	0.5, 1.1
≥500	48	96	0.7	0.4, 1.0	25	96	0.7	0.4, 1.2
Cumulative use adjusted for hands-free use (hours)								
<30	53	108	0.8	0.5, 1.1	32	108	0.6	0.4, 0.9
30–499	99	173	0.8	0.6, 1.1	54	172	0.7	0.5, 1.1
≥500	42	84	0.6	0.4, 1.0	22	85	0.7	0.4, 1.2
Cumulative no. of calls								
<650	49	98	0.8	0.5, 1.2	27	98	0.5	0.3, 0.9
650–8,549	100	192	0.8	0.5, 1.1	56	192	0.7	0.5, 1.0
≥8,550	48	94	0.7	0.4, 1.0	25	94	0.8	0.5, 1.3
Digital phones								
Regular use§	205	388	0.8	0.6, 1.0	111	388	0.6	0.5, 0.9
Time since first regular use (years)								
<5	119	243	0.7	0.5, 1.0	66	240	0.6	0.4, 0.9
≥5	83	136	0.8	0.6, 1.2	43	139	0.8	0.5, 1.2
Analog phones								
Regular use§	59	96	0.8	0.5, 1.2	26	96	0.7	0.4, 1.3
Time since first regular use (years)								
<5	9	12	1.0	0.4, 2.6	3	12	0.6	0.2, 2.3
5–9	25	44	0.7	0.4, 1.2	11	46	0.7	0.3, 1.4
≥10	25	38	0.8	0.5, 1.5	12	36	0.9	0.5, 2.0

* Adjusted for age, gender, geographic region, and education.
† Note: Totals for variables are not equal because of missing responses to several questions.
‡ Referent category.
§ "Regular use" defined as use of a mobile phone on average once per week or more, during 6 months or more.

continuously throughout the study period and adjustment of controls' referent dates ensured that controls did not have a longer opportunity for exposure than cases. All contacts and personal interviews were performed by trained nurses and a psychologist, ensuring professional and standardized treatment of cases and controls.

Participation rates were similar to what is generally found in Swedish case-control studies. Nevertheless,

TABLE 3. Odds ratios* of glioma and meningioma in the parietal/temporal, frontal, and other lobes according to mobile phone use, Sweden, 2000–2002†

	No. of controls	Parietal/temporal lobe			Frontal lobe			Other lobes		
		No. of cases	Odds ratio	95% confidence interval	No. of cases	Odds ratio	95% confidence interval	No. of cases	Odds ratio	95% confidence interval
Glioma										
Never or rarely‡	275	87	1.0		47	1.0		14	1.0	
Regular use§	399	117	0.8	0.6, 1.1	62	0.7	0.4, 1.1	23	0.8	0.4, 1.7
Duration of regular use (years)										
<5	219	65	0.9	0.6, 1.3	32	0.6	0.4, 1.1	15	1.2	0.5, 2.7
5–9	138	38	0.7	0.4, 1.1	23	0.7	0.4, 1.3	6	0.5	0.2, 1.4
≥10	33	12	0.8	0.4, 1.7	7	1.0	0.4, 2.5	2	0.7	0.2, 3.5
Time since first regular use (years)										
<5	213	63	0.9	0.6, 1.3	29	0.6	0.4, 1.0	12	1.0	0.4, 2.3
5–9	139	39	0.7	0.4, 1.1	26	0.8	0.5, 1.5	8	0.7	0.3, 1.7
≥10	38	14	0.8	0.4, 1.6	7	0.9	0.4, 2.2	3	0.9	0.2, 3.6
Meningioma										
Never or rarely‡	275	57	1.0		58	1.0		26	1.0	
Regular use§	399	32	0.5	0.3, 0.8	53	0.8	0.5, 1.2	17	0.6	0.3, 1.2
Duration of regular use (years)										
<5	220	24	0.6	0.3, 1.0	29	0.8	0.5, 1.3	10	0.6	0.2, 1.2
5–9	138	7	0.4	0.1, 0.8	22	1.0	0.6, 1.9	3	0.4	0.1, 1.3
≥10	32	1	0.2	0.0, 1.8	2	0.4	0.1, 1.8	3	1.7	0.4, 6.3
Time since first regular use (years)										
<5	213	21	0.5	0.3, 0.9	26	0.7	0.4, 1.2	9	0.5	0.2, 1.2
5–9	141	9	0.5	0.2, 1.0	22	1.0	0.6, 1.8	4	0.5	0.2, 1.5
≥10	36	2	0.4	0.1, 2.0	5	0.9	0.3, 2.5	3	1.5	0.4, 5.8

* Adjusted for age, gender, geographic region, and education.

† Note: Totals for variables are not equal because of missing responses to several questions; 21 glioma cases and 30 meningioma cases were excluded in the analyses because of missing information on detailed tumor location.

‡ Referent category.

§ Regular use defined as use of a mobile phone on average once per week or more, during 6 months or more.

nonparticipation is a source of potential selection bias. If mobile phone users were more willing to participate than nonusers, the risk might be underestimated. To test this problem, individuals that declined participation when contacted by phone were asked if they had regularly used a mobile phone. Among controls who refused participation, 34 percent reported regular use compared with 59 percent among participating controls. The corresponding numbers for cases were 50 percent and 52 percent, respectively. On the other hand, only 18 percent of the nonparticipating controls and only 13 percent of the nonparticipating cases answered the question. Among those whom we were unable to contact, mobile phone use might be more prevalent; these subjects were either not at home when we on numerous occasions tried to reach them or had unlisted telephone numbers. It is, however, possible that nonparticipation among controls might explain why the observed odds ratios are slightly less than 1.0. Mobile phone use was more frequent among men than women, especially long-term use, and meningioma is more common among women. This could explain the lower proportion of mobile phone users among meningioma cases.

Differential misclassification of the exposure is a potential problem, since mobile phone use is self-reported and recall of past mobile phone use may be difficult, especially for long-term use. The disease might have had some impact on

TABLE 4. Odds ratios* of low-grade (I–II) and high-grade (III–IV) glioma and glioblastoma according to mobile phone use, Sweden, 2000–2002†

	No. of controls	Glioma I–II			Glioma III–IV			Glioblastoma		
		No. of cases	Odds ratio	95% confidence interval	No. of cases	Odds ratio	95% confidence interval	No. of cases	Odds ratio	95% confidence interval
Frequency of use										
Never or rarely‡	275	29	1.0		117	1.0		80	1.0	
Regular use§	399	44	0.6	0.3, 1.0	155	0.9	0.6, 1.2	94	0.8	0.5, 1.2
Duration of regular use (years)										
<5	219	25	0.6	0.3, 1.1	86	0.9	0.7, 1.3	51	0.9	0.6, 1.3
5–9	138	13	0.5	0.2, 1.0	53	0.8	0.5, 1.2	33	0.7	0.4, 1.2
≥10	33	6	1.1	0.4, 3.1	14	0.8	0.4, 1.6	9	0.8	0.4, 1.8
Time since first regular use (years)										
<5	213	22	0.6	0.3, 1.1	83	0.9	0.7, 1.4	50	0.9	0.6, 1.3
5–9	139	16	0.6	0.3, 1.2	55	0.8	0.5, 1.2	35	0.8	0.5, 1.2
≥10	38	6	1.0	0.4, 2.8	16	0.8	0.4, 1.5	9	0.7	0.3, 1.6
Cumulative use (hours)										
<30	105	8	0.5	0.2, 1.2	38	0.9	0.6, 1.4	24	0.9	0.5, 1.4
30–499	182	21	0.7	0.4, 1.3	71	0.8	0.6, 1.2	46	0.8	0.5, 1.3
≥500	96	12	0.5	0.2, 1.2	33	0.7	0.4, 1.1	18	0.5	0.3, 1.1
Cumulative use adjusted for hands-free use (hours)										
<30	108	9	0.5	0.2, 1.2	39	0.8	0.5, 1.3	24	0.8	0.5, 1.3
30–499	173	22	0.7	0.4, 1.3	71	0.9	0.6, 1.3	46	0.8	0.5, 1.3
≥500	84	10	0.5	0.2, 1.1	29	0.7	0.4, 1.1	15	0.5	0.3, 1.0
Cumulative no. of calls										
<650	98	10	0.7	0.3, 1.6	35	0.9	0.5, 1.4	23	0.9	0.5, 1.5
650–8,549	192	19	0.6	0.3, 1.1	73	0.8	0.6, 1.2	45	0.8	0.5, 1.2
≥8,550	94	12	0.5	0.2, 1.2	34	0.7	0.4, 1.2	20	0.7	0.3, 1.2

* Adjusted for age, gender, geographic region, and education.

† Note: Totals for variables are not equal because of missing responses to several questions; 26 cases are excluded because of missing information on tumor histology.

‡ Referent category.

§ "Regular use" defined as use of a mobile phone on average once per week or more, during 6 months or more.

cases' ability to recall past events and habits as accurately as healthy persons recall these. However, the results from the quality assessment of the interviews did not indicate that the observed odds ratios were related to the interview quality, and cases and controls needed on average the same amount of time to complete the interview. Furthermore, impairment of memory is less common in young and middle-aged patients than in elderly patients (17). Long-term mobile phone use is most common among young and middle-aged persons.

The slightly increased odds ratio for glioma and meningioma associated with duration of years of ipsilateral mobile phone use could not be verified in the analysis of ipsilateral mobile phone use restricted to the temporal or parietal lobes. If there is a causal association between radiofrequency exposure from mobile phone use and brain tumors, we would have expected the highest odds ratio in the analysis restricted to the temporal or parietal lobes where the exposure from the mobile phone is highest. This, together with the finding of a decreased odds ratio for contralateral mobile phone use, indicates that recall bias may have affected these results. It is not biologically plausible that radiofrequency exposure from mobile phone use would

TABLE 5. Odds ratios* of glioma and meningioma according to laterality of tumors in relation to laterality of mobile phone use, Sweden, 2000–2002†

	Glioma				Meningioma			
	No. of cases	No. of controls	Odds ratio	95% confidence interval	No. of cases	No. of controls	Odds ratio	95% confidence interval
Ipsilateral exposure‡								
Referent category	192	443	1.0		159	443	1.0	
Regular use§	117	228	1.1	0.8, 1.5	49	228	0.8	0.5, 1.1
Duration of regular use (years)								
<5	68	129	1.2	0.8, 1.7	30	129	0.7	0.5, 1.2
5–9	34	76	0.9	0.6, 1.4	15	76	0.8	0.4, 1.5
≥10	14	15	1.8	0.8, 3.9	4	15	1.4	0.4, 4.4
Time since first regular use (years)								
<5	64	124	1.1	0.8, 1.6	27	124	0.7	0.4, 1.1
5–9	38	78	1.0	0.6, 1.5	17	78	0.9	0.5, 1.6
≥10	15	18	1.6	0.8, 3.4	5	18	1.3	0.5, 3.9
Contralateral exposure¶								
Referent category	224	459	1.0		168	459	1.0	
Regular use§	85	212	0.7	0.5, 1.0	40	212	0.6	0.4, 0.9
Duration of regular use (years)								
<5	36	108	0.6	0.4, 1.0	23	109	0.6	0.4, 1.0
5–9	39	79	0.9	0.6, 1.3	14	79	0.6	0.3, 1.2
≥10	9	23	0.6	0.3, 1.4	3	22	0.5	0.1, 1.8
Time since first regular use (years)								
<5	33	107	0.6	0.4, 0.9	19	107	0.5	0.3, 0.9
5–9	40	78	0.9	0.6, 1.4	18	80	0.8	0.5, 1.5
≥10	11	25	0.7	0.3, 1.5	3	23	0.5	0.1, 1.7

* Adjusted for age, gender, geographic region, and education.

† Totals for variables are not equal because of missing responses to several questions. Ten glioma cases, four meningioma cases, and three controls did not state on which side of the head they generally held the phone and were therefore excluded in the analysis; 21 glioma cases and 25 meningioma cases were excluded because of missing information on tumor side, and 31 glioma cases and 36 meningioma cases were excluded because tumors were located on both sides of the head or only in the midsection.

‡ "Exposure" defined as phone use on the same side as the tumor or on both sides, and "referent category" as never or rare use of any type of mobile phone and use on the opposite side of the tumor.

§ "Regular use" defined as use of a mobile phone on average once per week or more, during 6 months or more.

¶ "Exposure" defined as phone use on the opposite side of the tumor or on both sides, and "referent category" as never or rare use of any type of mobile phone and use on the same side as the tumor.

increase the brain tumor risk on the side of the head where the phone is usually held and protect against brain tumors on the opposite side of the head.

Some previous studies have used a laterality analysis restricted to cases only, to describe the association between laterality of the tumor and laterality of phone use, assuming an even distribution of the tumors on both sides of the head (14, 16). We randomly distributed our controls into two control groups and analyzed left-side and right-side tumors separately. Thus, these laterality analyses can be viewed as two separate case-control studies, where exposure in one study was defined as mobile phone use on the left side of the head and, in the other, defined as right-side use. A person could only be included in either the left-side analyses or the right-side analyses. Persons who used the phone on both sides are exposed in both substudies. Our data show that they are more extensive mobile phone users than persons who use the phone on only one side; the median number of hours of phone use was 293 hours for persons using both sides compared with 112 hours for persons who use the phone on only one side. The results from the two studies were pooled into one odds ratio.

No previously reported study has found any association between mobile phone use and meningioma (3, 4, 13–16), and the majority of the studies report similar results for glioma (13–16). Some associations with glioma have been reported (3, 4), but there are methodological considerations that limit the interpretability of these few positive findings. The Finnish study (3) that reported an increased risk of glioma among analog mobile phone users after only 2

TABLE 6. Odds ratios* of glioma and meningioma according to laterality of temporal and parietal tumors in relation to laterality of mobile phone use, Sweden, 2000–2002†

	Glioma				Meningioma			
	No. of cases	No. of controls	Odds ratio	95% confidence interval	No. of cases	No. of controls	Odds ratio	95% confidence interval
Ipsilateral exposure‡								
Referent category	123	443	1.0		65	443	1.0	
Regular use§	70	228	1.0	0.7, 1.4	16	228	0.6	0.3, 1.1
Duration of regular use (years)								
<5	44	129	1.2	0.8, 1.8	13	129	0.8	0.4, 1.5
5–9	18	76	0.7	0.4, 1.2	3	76	0.3	0.1, 1.1
≥10	7	15	1.1	0.4, 2.9	0	15		
Time since first regular use (years)								
<5	42	124	1.2	0.8, 1.9	12	124	0.7	0.4, 1.4
5–9	20	78	0.8	0.5, 1.4	3	78	0.4	0.1, 1.3
≥10	8	18	1.1	0.5, 2.7	1	18	0.7	0.1, 5.5
Contralateral exposure¶								
Referent category	141	459	1.0		69	459	1.0	
Regular use§	52	212	0.7	0.5, 1.1	12	212	0.5	0.2, 0.9
Duration of regular use (years)								
<5	22	108	0.7	0.4, 1.2	8	109	0.5	0.2, 1.1
5–9	24	79	0.8	0.5, 1.4	3	79	0.4	0.1, 1.3
≥10	5	23	0.5	0.2, 1.5	1	22	0.5	0.1, 3.9
Time since first regular use (years)								
<5	22	107	0.7	0.4, 1.2	6	107	0.4	0.2, 0.9
5–9	23	78	0.8	0.5, 1.4	5	80	0.6	0.2, 1.6
≥10	6	25	0.6	0.2, 1.5	1	23	0.5	0.1, 3.9

* Adjusted for age, gender, geographic region, and education.

† Totals for variables are not equal because of missing responses to several questions. Four glioma cases, one meningioma case, and three controls did not state on which side of the head they generally held the phone and were therefore excluded in the analysis. Seven glioma cases and seven meningioma cases were excluded because tumors were located on both sides of the head.

‡ "Exposure" defined as phone use on the same side as the tumor or on both sides, and referent category as never or rare use of any type of mobile phone and use on the opposite side of the tumor.

§ "Regular use" defined as use of a mobile phone on average once per week or more, during 6 months or more.

¶ "Exposure" defined as phone use on the opposite side of the tumor or on both sides, and "referent category" as never or rare use of any type of mobile phone and use on the same side as the tumor.

years of use was a register-based, case-control study with limitation in exposure assessment. If exposure to radiofrequency fields from mobile phones has a short-term promotional effect on glioma development, we would have expected to see an increase in the incidence of intracranial tumors among young or middle-aged men during the end of the 1990s. A descriptive epidemiologic study of intracerebral tumors did not report any indication of such increase in the Nordic countries (18). The incidence trend of glioma for both men and women was reported to be stable for those aged 20–59 years during increasing prevalence of mobile phone use. A Swedish case-control study (4) has also reported an increased risk of glioma, but the study has been criticized for limitations in methods, analysis, and presentation of the study (2, 19).

Limitations of previous epidemiologic studies (3, 4, 13–16) are the small number of individuals with long-term exposure and the lack of power to study the effects of long-term mobile phone use. Current knowledge about human cancer development indicates that the period from first exposure to clinical detection of the cancer can be more than 10 years and sometimes even more than 20 years (5). Given that mobile phone use increases the risk of cancer, a risk increase cannot be observed until several years after first exposure. However, if radiofrequency radiation acts as a promoter, an effect could possibly be seen after a shorter

duration of mobile phone use. Our Swedish study, which includes a large number of long-term mobile phone users, does not support the few previously reported positive findings and does not indicate any risk increases for either short-term or long-term exposures.

Our previously reported results for acoustic neuroma, indicating an increased risk related to mobile phone use of at least 10 years' duration, were confined to the side of the head where the phone was usually held (7). Results for contralateral use did not indicate recall bias when cases reported side of use, as was the case in the results for brain tumors presented here. The lack of association for glioma and meningioma speaks against underreporting of mobile phone use among controls as an explanation for the acoustic neuroma findings, which strengthens the finding of an increased risk for acoustic neuroma.

We conclude that these data do not support the hypothesis that mobile phone use is related to an increased risk of glioma or meningioma. It is, however, important to note that a carcinogenic effect after a very long induction time would remain undetected.

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