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Original Contribution

Cellular Phones, Cordless Phones, and the Risks of Glioma and Meningioma (Interphone Study Group, Germany)

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The widespread use of cellular telephones has generated concern about possible adverse health effects, particularly brain tumors. In this population-based case-control study carried out in three regions of Germany, all incident cases of glioma and meningioma among patients aged 30–69 years were ascertained during 2000–2003. Controls matched on age, gender, and region were randomly drawn from population registries. In total, 366 glioma cases, 381 meningioma cases, and 1,494 controls were interviewed. Overall use of a cellular phone was not associated with brain tumor risk; the respective odds ratios were 0.98 (95% confidence interval (CI): 0.74, 1.29) for glioma and 0.84 (95% CI: 0.62, 1.13) for meningioma. Among persons who had used cellular phones for 10 or more years, increased risk was found for glioma (odds ratio = 2.20, 95% CI: 0.94, 5.11) but not for meningioma (odds ratio = 1.09, 95% CI: 0.35, 3.37). No excess of temporal glioma ($p = 0.41$) or meningioma ($p = 0.43$) was observed in cellular phone users as compared with nonusers. Cordless phone use was not related to either glioma risk or meningioma risk. In conclusion, no overall increased risk of glioma or meningioma was observed among these cellular phone users; however, for long-term cellular phone users, results need to be confirmed before firm conclusions can be drawn.

brain neoplasms; cellular phone; electromagnetic fields; glioma; meningioma; telephone

Abbreviations: CI, confidence interval; DECT, digital enhanced cordless telecommunications; GSM, Global System for Mobile Communications.

The widespread use of cellular telephones throughout the world has raised concern about possible adverse health effects (1). During operation, cellular phones emit microwave radiation, which is absorbed by the brain (2). Hence, brain tumors are of particular concern. The possible association between cellular phone use and risk of brain tumors has been investigated in a number of epidemiologic studies, with inconsistent results (3–9). To avoid problems associated with discrepancies between study designs, the Interphone Study, an international collaborative case-control study of the relation between brain tumors and cellular phone use, has been set up in 13 countries (10). The first national reports from this study (from Denmark and Sweden) suggested no increased risk of glioma or meningioma among regular cellular phone users (11, 12).

In Germany, mobile telephony in the general population is a rather recent phenomenon. There are currently four network operators providing cellular phone systems in

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Germany, all with nationwide coverage. Of the four digital networks (Global System for Mobile Communications (GSM)), two operate mainly in the 900-MHz band and two operate in the 1,800-MHz band only. The GSM systems have operated since late 1992 and became widespread in the mid-1990s. By the end of 2004, there were more than 60 million cellular phone subscribers. The last analog system, the C Net system (Deutsche Telekom AG, Bonn, Germany), operating at 450 MHz, was introduced in 1985 but never had more than a million users and was shut down in 2001. Only about 10 percent of these phones were used as personal cellular phones, since most of the C Net mobile phones were car phones. In the 1990s, cordless phones became very popular in Germany and are now replacing the common fixed-line phones. Digital enhanced cordless telecommunications (DECT), with an operating frequency in the 1,900-MHz band, is now the digital technical standard and dominates the market. Compared with a maximum output power of 2 W (900 MHz) and 1 W (1,800 MHz) for the GSM phones, the maximum output power of a DECT cordless phone (0.25 W) is lower; however, the total duration of use of DECT phones may be longer than that for cellular phones.

Our aim in this study was to examine whether the risk of glioma or meningioma is associated with the use of cellular phones or cordless phones.

MATERIALS AND METHODS

The German part of the Interphone Study follows the international core protocol (10). It is not a nationwide study but a population-based study centered in the areas around Bielefeld, Mainz, Heidelberg, and Mannheim (covering approximately 6.6 million inhabitants (data provided by the Federal Office of Statistics)). Ethical clearance was obtained from the ethical commissions of the German states of Baden-Württemberg, North Rhine-Westphalia, and Rhineland-Palatinate.

Subjects

All incident cases of glioma and meningioma for which patients were referred to the neurosurgical clinics in Bielefeld, Heidelberg, Mainz, and Mannheim were ascertained. These four large clinics cover the metropolitan areas and rural surroundings of these cities. Cases were eligible for the study if their tumor was diagnosed between October 15, 2000, and October 31, 2003, they were aged 30–59 years on the date of diagnosis, and they lived within the study region on the date of diagnosis. In 2001, additional national funding was allocated to increase the sample size for the German part of the Interphone Study; thus, incident cases among persons aged 60–69 years with diagnosis dates after October 1, 2001, were also ascertained. In Germany, among patients aged 30–69 years, it is state-of-the-art to confirm the diagnosis by histology with a stereotactic biopsy or during surgery. Therefore, cases without histologic confirmation of their tumor (22 cases in total) were excluded. Other exclusion criteria were recurrent tumors, prevalent tumors with at least conclusive imaging or histologic confirmation before the start of the ascertainment period, insufficient knowledge of the German language, or main residence outside the study region. All cases were identified by study staff, who visited the neurosurgical clinics at least twice per week. The files of the neuropathology departments of the four study clinics were regularly checked to ensure that no cases were missed. Before a patient was approached, the physician responsible for treatment was asked to confirm eligibility and to approve contact with the patient or his or her family. No case was excluded because of the physician's preference. The vast majority of cases were contacted directly at the clinic. Most agreed to be interviewed during their stay at the hospital. Proxy interviews were conducted if the case had died or was too ill to perform the interview.

Controls were randomly selected from the population registries in the defined study region. Registration is compulsory in Germany; hence, these computerized registries are virtually complete, are updated on a monthly basis, and contain information on name, address, date of birth, and gender. Controls were drawn according to the gender, age, and regional distribution of the eligible cases and were frequency-matched to participating cases. If a control refused to participate, a substitute was sampled. Controls received an invitation letter and, if they did not respond, a reminder letter 2–4 weeks later. Nonresponders to the reminder letter were then approached by telephone. Controls were excluded if they had moved out of the study region or had died just before the sampling date (so their address was still in the population registry), if their knowledge of the German language was insufficient to perform the interview, or if their main residence was outside the study region. Controls who replied to the invitation letter were contacted by telephone to arrange an appointment for the interview, which was almost always conducted in the control's home. If a control was too ill to participate or had died after sampling, the family was approached for a proxy interview.

In all, response rates of more than 80 percent among cases and more than 60 percent among controls were achieved. Details on participation and the proportions of proxy interviews are shown in table 1. Less than 5 percent of the glioma and meningioma patients but 30 percent of the controls refused to be interviewed. Among glioma cases, 27 proxies were husbands or wives, 11 were sons or daughters, and two were siblings. Among meningioma cases, two proxies were spouses and three were sons or daughters. Among controls, five proxies were spouses and one was a daughter. Because we performed post-hoc 1:2-person matching before analyses, 41 controls had no matching partner and were therefore not included in the analyses (see ''Statistical methods'' section below).

Exposure assessment

Face-to-face interviews were conducted with a computerized questionnaire specifically developed for the Interphone Study. Respondents were asked whether they had ever used a cellular phone. If so, they were asked whether they were regular users (defined as at least one incoming or outgoing call per week for 6 months or more) and about their history of cellular phone use, including make and model. For each cellular phone used regularly, starting and cessation dates of

TABLE 1. Rates of participation in a German case-control study on cellular phone use and risks of glioma and meningioma, 2000–2003

	Glioma cases		Meningioma cases		Controls	
	No.	%	No.	%	No.	%
Eligible	460	100.0	431	100.0	2,449	100.0
Refused	22	4.8	21	4.9	747	30.5
Lost to follow-up	6	1.3	9	2.1	118	4.8
Died	42	9.1	4	0.9	1	0.0
Too ill	24	5.2	16	3.7	48	2.0
Participants	366	79.6	381	88.4	1,535	62.7
No match partner	0		0		41	
Included in analyses	366	100.0	381	100.0	1,494	100.0
Proxy interview	40	10.9	5	1.3	6	0.4

use were recorded. If the respondent was still using the cellular phone on the day of the interview, the cessation date was set to the date of diagnosis (for cases) or the reference date (for controls; date of diagnosis of the matched case). The questionnaire also contained questions on the numbers of calls made and received and on the duration of calls on each cellular phone and changes in patterns of use which were sustained for 6 months or more. On the basis of this information, the lifetime number of calls and the lifetime hours of cellular phone use were estimated. For each cellular phone, information on use of headsets with a microphone (hands-free devices) and use of hands-free sets in vehicles was obtained. This information was used to modify the exposure estimate (see below). Questions regarding cordless phones were also asked during the face-to-face interview using a separate paper questionnaire. The questions addressed the technical standard of the cordless phone (DECT or analog), the make and model, the starting and stopping dates of cordless phone use, and the location of the base station within the house or apartment.

Statistical methods

At the end of data collection, we performed post-hoc 1:2-person matching by assigning two controls to each case, matched on sex, birth year (± 2 years), and region (Bielefeld, Mainz, and Heidelberg/Mannheim, with a few exceptions), to adjust for the time lag in interviewing cases and controls. By means of this method, we censored the exposure period of the controls at the date of diagnosis of the matched case. This is particularly necessary for analysis of exposures changing rapidly over time, such as the use of cellular phones; otherwise the time lag would lead to overestimation of cellular phone use among controls. Post-hoc matching completely accounted for this potential bias, since we obtained a distribution of reference dates among controls that was identical to the distribution of diagnosis dates among cases.

The following exposure metrics were constructed for analyses: ever having been a regular user (as defined above) versus never; years since first regular use of a cellular phone; lifetime number of calls, modified for the use of hands-free devices; lifetime hours of cellular phone use, modified for the use of hands-free devices; intensity of use (average number of minutes spent on a cellular phone per day); and total hours of cellular phone use in certain time windows. The number of calls and the duration of calls were reduced by 100 percent, 75 percent, 50 percent, or 25 percent for periods in which the subject reported corresponding use of hands-free devices. In further analysis, we compared distributions of tumor locations between exposed and unexposed cases. In an additional regression analysis, we modeled the probability of having a temporal tumor as a function of exposure from cellular phone use, gender, age, and tumor grade (gliomas).

In the main model, conditional logistic regression analyses for frequency-matched data sets were used to estimate the odds ratio and its respective 95 percent confidence interval (13). All analyses were stratified by gender and study center (Bielefeld, Heidelberg/Mannheim, or Mainz) and additionally adjusted for age at the reference date (by year), socioeconomic status (low, intermediate, or high), and living in a city ($\geq$100,000 inhabitants vs. $<$100,000). The definition of socioeconomic status was one commonly used in German epidemiologic studies; it is based on the highest school qualification and the highest level of occupational or academic training (14).

In sensitivity analyses, unadjusted odds ratios as well as odds ratios from conditional logistic regression of individually matched data were calculated. Both approaches showed only minor differences with the main approach, so only the results from the main model are reported. Cutoff points used in the analysis were all based on the distribution of exposure among controls. In analyses using number of calls or duration of calls, proxy interviews were excluded.

RESULTS

Table 2 shows the demographic characteristics of cases and controls. There were no major differences between cases

TABLE 2. Demographic characteristics (%) of cases and controls in a German case-control study on cellular phone use and risks of glioma and meningioma, 2000–2003

	Glioma		Meningioma	
	Cases ($n = 366$)	Controls ($n = 732$)	Cases ($n = 381$)	Controls ($n = 762$)
Gender				
Male	59.0	59.0	27.0	27.0
Female	41.0	41.0	73.0	73.0
Age group (years)*				
≤39	16.4	16.7	10.2	10.1
40–49	22.7	23.6	20.5	21.8
50–59	30.9	28.6	34.9	34.0
≥60	30.1	31.1	34.4	34.1
Study center				
Bielefeld	27.3	27.7	26.0	26.8
Heidelberg/ Mannheim	48.9	47.7	50.7	48.4
Mainz	23.8	24.6	23.4	24.8
Socioeconomic status†				
Low	7.1	4.8	9.7	7.1
Average	59.3	59.2	62.5	59.4
High	33.6	36.1	27.8	33.5
City resident (≥100,000 inhabitants)				
No	74.9	77.6	73.5	77.4
Yes	25.1	22.4	26.5	22.6
Smoking status				
Never smoker	46.2	41.1	50.4	48.8
Ex-smoker	26.2	28.7	25.5	26.5
Current smoker	27.6	30.2	24.2	24.8

* In interpreting the age distribution, one must keep in mind that the recruitment period for patients aged 30–59 years was 3 years but that for patients aged 60–69 years was only 2 years.

† The definition of socioeconomic status was based on the highest school qualification and the highest level of occupational or academic training (14).

and controls with regard to age at the reference date, study region, or living in a city. The proportion of subjects with a low socioeconomic status was somewhat higher among cases. The proportions of current smokers were similar for cases and controls.

Table 3 shows the results of the main analyses. There was no increased risk of glioma or meningioma for most of the exposure measurements. Among long-term cellular phone users (≥10 years), however, a twofold risk of glioma was observed. In addition to the results presented in table 3, a trend analysis by year of cellular phone use, using nonregular users and short-term users (<5 years since time of first use) as the reference group, revealed odds ratios of 1.06 (95 percent confidence interval (CI): 0.98, 1.15) for glioma and 1.00 (95 percent CI: 0.87, 1.14) for meningioma.

Information obtained from proxies was included in analyses of regular cellular phone use and years since first regular use. Omitting proxy interviews from these analyses only marginally altered the results: For regular cellular phone use, the odds ratios were 0.97 (95 percent CI: 0.72, 1.30) for glioma and 0.83 (95 percent CI: 0.62, 1.12) for meningioma. The odds ratios for long-term users were 2.03 (95 percent CI: 0.84, 4.92) for glioma and 1.09 (95 percent CI: 0.35, 3.37) for meningioma. The amount of cellular phone use was corrected for the use of hands-free devices in all analyses; however, the majority of subjects never used such devices. For the glioma analysis, 79 percent of both cases and controls reported that they never used a headphone or a hands-free kit in a car. The respective fractions in the meningioma analysis were even higher: 88 percent among cases and 85 percent among controls. In total, only 2 percent of all subjects reported that they always used hands-free devices when making or receiving calls.

Some subgroup analyses were planned in advance, namely analyses stratified by glioma grade (division into low-grade and high-grade, since the etiologies might differ) and by gender (the incidence of different brain tumor types varies considerably by gender, with a preponderance of males among gliomas and a preponderance of females among meningiomas (15, 16)). As table 4 shows, no gender differences were observed for meningioma cases or for low-grade gliomas, but among high-grade gliomas, there was an increased risk in females (odds ratio = 1.96, 95 percent CI: 1.10, 3.50). This finding was accompanied by a weak trend of increasing risk with increasing time since first regular use of cellular phones. The respective odds ratios were 1.78 (95 percent CI: 0.93, 3.41) for 1–4 years since first regular use and 1.93 (95 percent CI: 0.69, 5.45) for 5 or more years since first regular use (p for trend = 0.06). Only one female glioma case (but no controls) had an exposure time of 10 years or more.

Since most of the energy of the microwave exposure incurred from use of cellular phones is absorbed within 3–4 cm of the brain in the immediate vicinity of the position at which the cellular phone is held, temporal brain tumors are of particular interest (2). In separate evaluations of low-grade and high-grade gliomas, regular cellular phone users had temporal tumors slightly less frequently than did nonregular cellular phone users; the proportions were 28 percent as compared with 35 percent for low-grade gliomas ($p = 0.54$) and 34 percent as compared with 39 percent for high-grade gliomas ($p = 0.35$). The analysis was repeated for subjects with a longer history of cellular phone use (≥5 years since the time of first regular use) compared with all others; the data showed a minor excess of temporal gliomas among the exposed (low-grade gliomas: 38 percent vs. 32 percent ($p = 0.71$); high-grade gliomas: 40 percent vs. 37 percent ($p = 0.74$)). Of 36 cases with a temporal high-grade glioma who were regular cellular phone users, 15 (42 percent) stated that they usually held the cellular phone on the side of the head of the tumor, while nine (25 percent) had no preferred side and 12 (33 percent) preferred the opposite side. Among the 37 high-grade glioma cases with a frontal tumor who were regular

TABLE 3. Patterns of cellular phone use and risks of glioma and meningioma in a case-control study, Germany, 2000–2003*

	Glioma				Meningioma			
	No. of cases	No. of controls	OR†	95% CI†	No. of cases	No. of controls	OR	95% CI
Regular‡ cellular phone use								
Never	228	449	1.00		277	528		
Ever	138	283	0.98	0.74, 1.29	104	234	0.84	0.62, 1.13
Time (years) since first regular use (three categories)§								
Never, <1	232	454	1.00		284	548	1.00	
1–4	82	187	0.87	0.63, 1.20	73	164	0.86	0.62, 1.20
≥5	51	91	1.12	0.75, 1.67	23	50	0.88	0.52, 1.51
Time (years) since first regular use (four categories)§								
Never, <1	232	454	1.00		284	548	1.00	
1–4	82	187	0.87	0.63, 1.20	73	164	0.86	0.62, 1.20
5–9	39	80	0.97	0.63, 1.50	18	41	0.84	0.47, 1.51
≥10	12	11	2.20	0.94, 5.11	5	9	1.09	0.35, 3.37
Lifetime no. of calls¶								
Never use	202	445	1.00		274	528	1.00	
≤1,176	56	125	0.99	0.68, 1.43	63	135	0.90	0.63, 1.28
>1,176, ≤4,350	24	81	0.66	0.40, 1.08	16	47	0.64	0.35, 1.17
>4,350	43	71	1.34	0.86, 2.07	21	51	0.76	0.44, 1.34
Lifetime duration of calls (hours)#								
Never use	202	445	1.00		274	528	1.00	
≤44	61	132	1.02	0.71, 1.45	61	130	0.91	0.64, 1.29
>44, ≤195	27	68	0.86	0.52, 1.41	14	56	0.47	0.25, 0.87
>195	34	74	1.01	0.64, 1.60	24	44	1.04	0.60, 1.81
Intensity of use (minutes/day)#								
Never use	202	445	1.00		274	528	1.00	
<30	108	254	0.93	0.69, 1.26	89	210	0.81	0.60, 1.11
≥30	14	20	1.54	0.75, 3.15	10	20	0.97	0.44, 2.17
Duration of calls ≥5 years before reference date**								
Never use	202	445	1.00		274	528	1.00	
<5 years	80	191	0.92	0.66, 1.27	78	184	0.81	0.59, 1.12
≥5 years, ≤34.5 hours	18	48	0.84	0.47, 1.50	10	19	1.01	0.46, 2.23
≥5 years, >34.5 hours	25	42	1.31	0.77, 2.26	13	31	0.78	0.39, 1.55

* Odds ratios from conditional logistic analysis for frequency-matched data sets, stratified by gender and study center and adjusted for age, socioeconomic status, and living in a city (see Materials and Methods).

† OR, odds ratio; CI, confidence interval.

‡ Regular use was defined as at least one incoming or outgoing call per week for 6 months or more.

§ There were missing values for one glioma case and one meningioma case.

¶ There were missing values or excluded proxies for 41 glioma cases, 10 glioma controls, seven meningioma cases, and one meningioma control.

There were missing values or excluded proxies for 42 glioma cases, 13 glioma controls, eight meningioma cases, and four meningioma controls.

** There were missing values or excluded proxies for 41 glioma cases, six glioma controls, and six meningioma cases.

cellular phone users, the respective figures were 16 (43 percent), six (16 percent), and 15 (41 percent), demonstrating no difference in this distribution in a less exposed area. In a multiple logistic regression model, the probability of having a temporal glioma was related only to age at diagnosis (with a higher probability with increasing age ($p = 0.03$)), not to gender ($p = 0.17$), tumor grade ($p = 0.95$), or regular cellular phone use ($p = 0.41$). The probability of

TABLE 4. Risks of glioma and meningioma among regular* cellular phone users, by gender and tumor grade, Germany, 2000–2003†

Regular cellular phone use	Low-grade glioma				High-grade glioma				Meningioma			
	No. of cases	No. of controls	OR‡	95% CI‡	No. of cases	No. of controls	OR	95% CI	No. of cases	No. of controls	OR	95% CI
Males												
Never	20	35	1.00		99	180	1.00		62	112	1.00	
Ever	21	47	0.89	0.38, 2.08	76	170	0.78	0.53, 1.14	41	94	0.77	0.45, 1.33
Females												
Never	35	64	1.00		74	170	1.00		215	416	1.00	
Ever	11	28	0.77	0.32, 1.84	30	38	1.96	1.10, 3.50	63	140	0.88	0.62, 1.26

* Regular use was defined as at least one incoming or outgoing call per week for 6 months or more.
† Odds ratios from conditional logistic analysis for frequency-matched data sets, stratified by study center and adjusted for age, socioeconomic status, and living in a city (see Materials and Methods).
‡ OR, odds ratio; CI, confidence interval.

having a temporal meningioma was not related to any of those factors, showing no statistically significant effects for gender ($p = 0.16$), age ($p = 0.42$), or cellular phone use ($p = 0.43$).

Table 5 shows the results for cordless phones. Cordless phones were more common than cellular phones; only 23.3 percent of control subjects did not use a cordless phone either at home or at work. No associations between the use of

TABLE 5. Risks of glioma and meningioma according to use of cordless phones and regular use of cellular phones, Germany, 2000–2003*

	Glioma				Meningioma			
	No. of cases	No. of controls	OR†	95% CI†	No. of cases	No. of controls	OR	95% CI
Cordless phone user‡								
No	93	173	1.00		107	174	1.00	
Yes (at home or at work)	270	557	0.93	0.69, 1.25	272	585	0.77	0.58, 1.03
Cordless phone user‡								
No	93	173	1.00		107	174	1.00	
Yes, at work only	6	12	0.98	0.35, 2.72	8	15	0.86	0.35, 2.11
Yes, at home only	223	463	0.92	0.68, 1.25	234	500	0.78	0.58, 1.04
Yes, at home and at work	41	82	0.97	0.61, 1.53	30	70	0.73	0.44, 1.20
Time (years) since first use (cordless phones)§								
No use or <1	118	214	1.00		130	215	1.00	
1–4	111	247	0.83	0.60, 1.14	112	244	0.76	0.56, 1.05
≥5	123	256	0.90	0.66, 1.23	128	281	0.78	0.57, 1.06
Time (years) since first use (cordless phones and/or cellular phones)¶								
No use or <1	81	156	1.00		96	175	1.00	
1–4	123	256	0.95	0.67, 1.35	133	256	0.97	0.69, 1.35
≥5	147	305	0.97	0.69, 1.37	140	309	0.86	0.62, 1.19

* Odds ratios from conditional logistic analysis for frequency-matched data sets, stratified by gender and study center and adjusted for age, socioeconomic status, and living in a city (see Materials and Methods).
† OR, odds ratio; CI, confidence interval.
‡ Data were missing for three glioma cases, two glioma controls, two meningioma cases, and three meningioma controls.
§ Data were missing for 14 glioma cases, 15 glioma controls, 11 meningioma cases, and 22 meningioma controls (use of cordless phones at home or at work).
¶ Data were missing for 15 glioma cases, 15 glioma controls, 12 meningioma cases, and 22 meningioma controls.

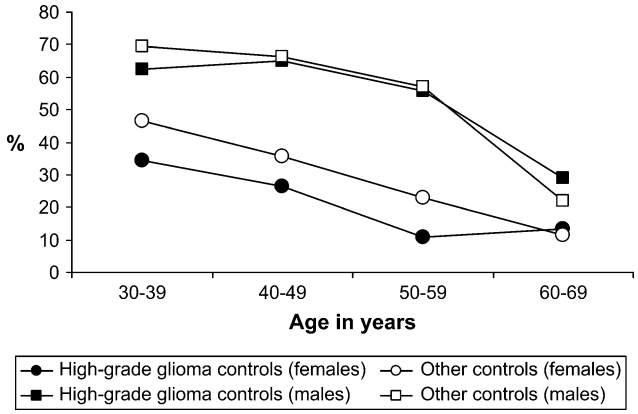

FIGURE 1. Prevalence of regular cellular phone use among controls matched to high-grade glioma patients as compared with controls matched to other patients, by age group and gender, Germany, 2000–2003.

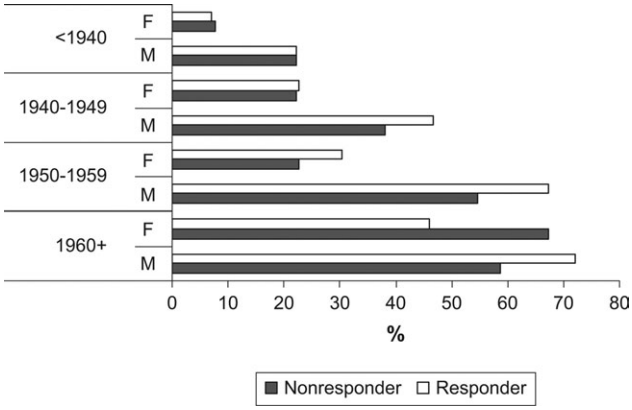

FIGURE 2. Proportions of cellular phone users among control participants and among nonparticipants who filled in the nonresponder questionnaire, by birth cohort and gender, Germany, 2000–2003. F, female; M, male.

cordless phones and the risks of glioma and meningioma were observed. Results were similar for both genders (data not shown).

DISCUSSION

The results of this study do not indicate an overall increased risk of glioma or meningioma among regular cellular phone users. These findings are consistent with the majority of previous studies on this topic (6, 7, 9, 11, 12). In a registry-based Finnish study, an association between glioma risk and short-term use of a cellular phone was observed (8). A Swedish study (3) and its extensions (4, 5) demonstrated an increased risk of all types of brain tumors among ever users of cellular phones. In this study, a reduced risk of meningioma was observed among moderate cellular phone users (particularly when exposure was measured by total duration of use), but this picture appeared to differ across the various exposure estimates. In the Danish and Swedish portions of the Interphone Study (11, 12), the estimated odds ratios for meningioma were also below 1.0, but no consistent pattern emerges when the three studies are compared.

In none of the previous studies has a gender-specific association been found, while a twofold increased risk of high-grade glioma was observed among women in this study. However, an examination of the prevalence of regular cellular phone use among female controls in the high-grade glioma group compared with the rest of the controls revealed a lower prevalence among high-grade glioma controls (figure 1). Because assignment to one of the two control groups was performed strictly randomly, this difference is rather unexpected; therefore, the increased risk of high-grade gliomas among women may be a chance finding. No such prevalence difference in the control groups was seen among men (figure 1).

A major finding of this study is that no excess of temporal tumors was observed, either for gliomas or for meningiomas. Since this is the area in the brain with the highest energy absorption of cellular phone emissions, one would expect more tumors to appear at these locations. Given the sample size of this study, however, only a crude analysis of distributions of tumor locations was feasible; such analysis will improve when data from all of the Interphone countries are pooled.

Only a few studies so far have included larger numbers of long-term cellular phone users. In this study, an increased risk of glioma but not of meningioma was observed among persons who had regularly used cellular phones for 10 years or more. The Danish and Swedish portions of the Interphone Study did not confirm this result (11, 12), while the other Swedish study showed a risk increase for all types of brain tumors (4, 5). In Germany, many long-term users were users of C Net, an analog system that was predominantly used by persons in certain occupations in which a transportable car phone was an advantage (17). After the digital GSM system was introduced in 1992, C Net rarely attracted new customers, and none of the study subjects who started to use a cellular phone after 1992 started as a user of the analog system. Hence, the findings for time since first use reflect the start of use with either the analog system or the digital system.

When we examined the observed risk of glioma among long-term users of cellular phones in greater detail, this result appeared to be very sensitive to the a-priori selected cutoff point at 10 years. At a cutoff point of 9 years or more, the odds ratio for glioma was 1.40 (95 percent CI: 0.68, 2.85). Furthermore, approximately half of the long-term cellular phone users (18 out of 37) reported subscribing to cellular phone systems that were not in operation at the time the interviewee reported having used the cellular phone. While we can only speculate as to whether the date of first use or the name of the network provider is more likely to be correct, this discrepancy indicates that such information is difficult to recall precisely during an interview.

In general, the potential impact of selection bias and recall bias needs to be discussed for all interview-based

case-control studies. While the refusal rate among cases was low in this study, it was much higher among controls, particularly among those of lower socioeconomic status. Since people with a more reserved attitude may be both more likely to refrain from regular cellular phone use and more likely to refuse to participate in a study like this, there may be a direct association between participation and the risk factor of interest, especially among controls. Because a short nonresponder questionnaire was included in the invitation letter and was filled in by 58 percent of nonresponding controls, this allowed for some comparisons between responders and nonresponders. Figure 2 shows the prevalence of cellular phone use among nonparticipants compared with that among participating controls, stratified by birth cohort and gender. As illustrated, there was a difference in the proportions of cellular phone users among men that was more marked with decreasing age, but there was no clear pattern among women. Since the proportion of cellular phone users among participating male controls was higher than that among nonresponders, this may explain the somewhat decreased risks for ever use of cellular phones (also shown by Lahkola et al. (18)).

In a validation study, interview data on current cellular phone use among volunteers were compared with data from the network operators, and fairly good agreement was observed (19, 20). It appeared from those data that the number of calls was slightly easier to recall than the duration of calls. Results for both number of calls and duration of calls are presented for this study, although, in theory, duration of calls better reflects cumulative exposure. However, this does not exclude the possibility that recall bias may pose a problem with respect to past cellular phone use or recall problems among patients with brain tumors. In the Danish study, patients with malignant glioma showed some performance problems on the Mini-Mental State Examination (11). In the Interphone Study, interviewers must rate the course of the questioning at the end of the interview. No major problems were reported for either cases or controls in our study; however, the accuracy of the given information is still difficult to evaluate.

The fact that most interviews with cases were conducted in a hospital while most controls were interviewed at home seems to be a potential source of bias on first sight. However, because most brain cancer patients have a long aftercare period after surgery and are rarely available at home, participation rates among cases living at home would have been much lower because of early postoperative deaths and refusals, introducing bias due to an association between participation and disease severity. Another possible limitation of the study is that early symptoms of the disease may have an impact on patterns of cellular phone use. If these symptoms include muscle weakness or paralysis on one side of the body, this may affect patterns of use. However, it is more likely that this would have affected laterality of use than amount of use, particularly the amount of use many years previously.

In contrast to a Swedish study (5), no association was observed in this study between cordless phone use and the risks of glioma and meningioma. While the output power level of cordless phones is much lower than that of cellular phones, the amount of use of cordless phones may be higher, since the costs associated with their use are much lower.

In conclusion, we observed no overall increased risk of glioma or meningioma among regular cellular phone users. With regard to the increased risk of high-grade glioma found among women only, other studies to date have not reported a similar effect; hence, this might have been a chance finding. There is also no supportive evidence regarding the tendency towards a reduced risk of meningioma seen among moderate cellular phone users in this study. The elevated risk of glioma after 10 or more years of cellular phone use also needs to be confirmed by other studies, since the number of long-term cellular phone users in this study was low and effects of recall bias cannot be ruled out. We found no excess of temporal gliomas or meningiomas among cellular phone users, but the spatial distribution of tumors within the brain will be examined in more detail when data from the entire Interphone Study are compiled.

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