Association of allergic diseases and epilepsy with risk of glioma, meningioma and acoustic neuroma: results of the INTERPHONE international case-control study

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Abbreviations

IARC/WHO	International Agency for Research on Cancer / World Health Organisation
ICD-O	International Classification of Diseases for Oncology
CI	95% confidence interval
OR	Odds ratio

Abstract

We investigated the association of allergic conditions and epilepsy with risk of brain tumours, in the 13-country Interphone case-control study. Data were obtained from 2693 glioma cases, 2396 meningioma cases, and 1102 acoustic neuroma cases and their 6321 controls. Conditional logistic regression models for frequency-matched data sets were used to estimate pooled odds ratios (ORs) and their respective 95% confidence intervals (CIs), adjusted for education and time at interview. Reduced ORs were observed for glioma in relation to physician's diagnosis of asthma (OR=0.73; CI 0.58-0.92), hay fever (OR 0.72; CI 0.61-0.86), and eczema (OR 0.78, CI 0.64-0.94), but not for meningioma or acoustic neuroma. Previous diagnosis of epilepsy was associated with an increased OR for glioma (2.94; CI 1.87-4.63) and for meningioma (2.12; CI 1.27-3.56), but not for acoustic neuroma. Findings from this large-scale case-control study add to the growing evidence that people with allergies have a lower risk of developing glioma, but not meningioma or acoustic neuroma. It also supports clinical observations of epilepsy prior to the diagnosis of glioma and meningioma.

Key words: allergies, epilepsy, brain tumours, multicenter case-control study

Introduction

Epidemiological studies have consistently found an inverse association between a history of allergic diseases and risk of glioma, while results were conflicting for meningioma and acoustic neuroma [1-3]. Underlying biological mechanisms appear to be complex; however, there is agreement that immunologic functions play an important role in the development of brain tumours, and allergic diseases probably indicate an effective immunosurveillance system [1, 2]. Epilepsy or epileptic seizures can occur as early symptoms of brain tumors and it has been hypothesized that seizure susceptibility increases due to interaction between tumor cell metabolism and the neuronal network [4, 5].

Interphone is an international multi-center case-control study carried out in 13 countries and coordinated by IARC/WHO [6]. It focused on the association between mobile phone use and brain tumours, but data on allergic diseases and epilepsy were also collected. Here we report the results of the pooled data set from the sixteen study centers on the associations between history of allergic diseases and epilepsy and risk of glioma, meningioma and acoustic neuroma.

Methods

The study population consists of incident, histologically or imaging-confirmed cases of glioma, meningioma and acoustic neuroma occurring between 2000 and 2004, 30-59 years old at diagnosis and their controls (one per case for glioma and meningioma, two per case for acoustic neuroma). Controls were matched on age, sex, and study region (for details see [6, 7]).

Interviews were performed by trained interviewers, mainly using a computer-assisted questionnaire, either face-to-face (93.9 % cases, 99.5 % controls) or by telephone. Proxy interviews were conducted when the participant was too ill or deceased. This was the case for 336 glioma cases, 41 meningioma cases, 3 acoustic neuroma cases and 40 controls. The interview comprised information on mobile phone use, ionizing and non-ionizing medical radiation exposures, socio-demographic factors and other potential risk factors for brain tumours. In addition, a history of various medical conditions, diagnosed by a physician, were asked, including the diagnoses of asthma, hay fever, or eczema; which are conditions thought to reflect allergic reactions. Details were asked about on the age at onset of these diseases, and for eczema the age when the symptoms stopped. Similar questions were asked for epilepsy.

Statistical approaches followed the strategy of all analyses of the Interphone study (for details see [6-7]). Conditional logistic regression models for frequency-matched data sets were used to estimate pooled odds ratios (ORs) and their 95% confidence intervals (CIs), adjusted for education and time interval between case and respective control interviews. Analyses were performed for each brain tumour type, and for men and women separately, or - if analysis was performed for men and women combined - adjusted for gender. Subgroup analyses were done separated for high-grade (type III-IV) and low-grade (type I and II) glioma, based on morphological codes of the ICD-O (details see [6, 7]).

Reference categories were defined as “never diagnosed with allergy” and ”never diagnosed with epilepsy”, respectively, as reported by the study subjects. Only diagnoses that occurred up to two years prior to the tumour diagnosis (cases) or reference date (controls; date of diagnosis

of corresponding case) were included. Missing data was less than 5% for epilepsy and less than 1% for the allergies.

For each asthma, hay fever, and eczema, we created a binary variable (ever/never). We also investigated whether time since first diagnosis (< 10 years, 10 - 19 years, ≥20 years) or age at onset (< 10 years, 10 – 19 years, ≥20 years) was associated with the diseases. For eczema, we distinguished past and current rash. We also estimated ORs for one or more than one allergy compared to no allergy. Sensitivity analyses were performed by excluding proxy interviews and by including smoking as a potential confounder, but there was no noticeable impact on the main results (data not shown).

Results

In total, the analyses included data from 2693 glioma cases (62.6% response rate), 2396 meningioma cases (76.9%) and 1102 acoustic neuroma cases (81.0%) and 6321 control subjects (44%). The distribution of cases and controls by selected demographic factors is presented in Supplementary Table 1. For all tumour types, educational level was slightly higher for controls than for cases.

For glioma, ORs below 1 were found for participants who were ever diagnosed with asthma (OR 0.73, CI 0.58-0.92), hay fever (OR 0.72, CI 0.61-0.86) or eczema (OR 0.78, CI 0.64-0.94), or "any allergy" (OR 0.71, CI 0.61-0.82) (Table 1). The result for eczema was driven by those with current rash. ORs were lowest when the allergies occurred less than ten years before glioma

tumour diagnosis, and in those where the allergies started in adulthood. Subdivision into high grade and low grade glioma showed that the decrease was driven by the results for high-grade glioma (Table 1). For meningioma, no association was seen in relation to asthma (OR 0.91, CI 0.72-1.14) or to hay fever (OR 0.91, CI 0.76-1.10), but eczema showed a slightly lower risk (OR 0.84, CI 0.70-1.02), more pronounced with current rash (OR 0.76; CI 0.60-0.95) (Table 1). For both tumour types there was little difference in ORs between men and women, however, for hay fever and eczema the ORs for men were somewhat lower (Table 2).

For acoustic neuroma no association was found with asthma (OR 1.02, CI 0.75-1.37), hay fever (OR 0.91, CI 0.72-1.14), or eczema (OR 1.02, CI 0.78-1.32), overall and by time since start of the allergy or by age of onset. The results were similar in men and women (Tables 1 and 2).

A prior diagnosis of epilepsy was associated with an increased OR for glioma (OR 2.94, CI 1.87-4.63) and for meningioma (OR 2.12, CI 1.27-3.56) (Table1). Subgroup analyses for glioma and meningioma and epilepsy were based on small numbers (Tables 1 and 2). However, for both glioma and meningioma, sex-specific analyses revealed higher risks for men than for women. The OR was higher for low-grade glioma (OR 5.71, CI 2.48-13.1) compared to high-grade glioma (OR 2.01, CI 1.14-3.54). For both glioma and meningioma, the highest ORs were seen for adult-onset epilepsy, and for subjects whose epilepsy was diagnosed less than 10 years before the reference date. ORs were not increased for acoustic neuroma (Table 1), however, analyses were based on small numbers of subjects with epilepsy.

Discussion

These analyses presents results using data from all Interphone study centers [6, 7]. Some differences in results published from single or smaller groups of study centers [e.g. 3, as most recent], may be due to chance or to differences in participation rates, prevalence of specific diseases or other factors.

Allergic diseases

We found inverse associations of asthma, hay fever and eczema with risk of glioma, especially for high-grade glioma, for both men and women. Allergic diseases diagnosed closer to the diagnosis of the high-grade glioma (less than 10 years) were associated with lower ORs than those diagnosed earlier and at early ages. Our findings are consistent with previous studies, as by comparison with results of a recent meta-analysis [8] and review [9]. Overall, no association was seen between low-grade glioma, meningioma, and acoustic neuroma with any of the three allergic diseases, which is in line with results of a nested case-control study using specific IgE as a biomarker for atopic sensitization [1]. Decreased ORs were observed, however, in subjects who reported at time of interview current eczema for low-grade glioma and for meningioma.

In addition, prospective studies have found lower levels of total or respiratory-specific immunoglobulin IgE, a biomarker of allergy, in glioma patients, strengthening our observation of an inverse association [1, 8]. The underlying biogenetic mechanism is not fully understood. The immediate hypersensitivity reactions of these three allergies are mediated by IgE, and this may be influenced by preclinical tumours. Further investigations of immunologic mechanisms,

for example in the immunosurveillance system, and investigations of germline SNPs or genetic risk factors are needed for better understanding of the mechanism [2].

History of Epilepsy

In line with earlier epidemiological studies and clinical observations, we found elevated ORs of glioma and meningioma in relation to past epilepsy with the highest ORs for low-grade glioma, a finding also described in other studies [4]. No association was seen between history of epilepsy and acoustic neuroma but numbers of subjects were small. Epilepsy and epileptic seizures prior, but close to the diagnosis of glioma or meningioma are known to be important symptoms of brain tumours as an early warning sign and prognostic factor for survival [5]. Different hypotheses concerning the epileptogenesis in tumour cells and peritumoral cells have been discussed, e.g. that an aberrant tumour cell metabolism may influence the neuronal network leading to seizures [4, 10].

Strengths and Limitations

This is to our knowledge the largest case-control study on this topic to date. With all centres following the same study protocol, no compromises had to be made when pooling the data. Participation proportions in cases (glioma 63%, meningioma 77% and acoustic neuroma 81%) were high and the distribution of cases by sex and age was as to be expected for the respective tumours types. For glioma, proxy interviews were used for 12% of cases, but excluding them had little impact on the results. Main limitations were the low response proportion among

controls and the fact that all data on medical diagnoses were based on self-reports of a physician's diagnosis, leading to concerns about potential selection and recall bias.

Conclusions

Findings from this large-scale, international case-control study with a representative distribution of cases for the respective tumour types, add to the growing evidence that people with allergies have a lower risk of glioma than those without allergies, especially for high-grade glioma, but not for meningioma or acoustic neuroma. It also confirms the association between epilepsy and glioma and meningioma, most likely due to epilepsy being a symptom in a sizeable proportion of these tumours.

References:

1. Schlehofer B, Siegmund B, Linseisen J, et al. Primary brain tumours and specific serum immunoglobulin E: a case-control study nested in the European Prospective Investigation into Cancer and Nutrition cohort. Allergy 2011; 66:1434-41. doi: 10.1111/j.1398-9995.2011.02670.x.

2. Ostrom QT, Bauchet L, Davis FG, et al. The epidemiology of glioma in adults : a « state of the science » review. Neuro-Oncology, 2014; 16:896-913. https://doi.org/10.1093/neuonc/nou087

3. Turner MC, Krewski D, Armstrong BK, et al. Allergy and brain tumors in the INTERPHONE study: pooled results from Australia, Canada, France, Israel, and New Zealand. Cancer Causes Control 2013; 24:949-60. doi: 10.1007/s10552-013-0171-7.

4. Vecht CJ, Kerkhof M, Duran-Pena A. Seizure prognosis in Brain Tumors : New Insights and Evidence-Based Management. The Oncologist. 2014; 19:751-759. http://dx.doi.org/10.1634/theoncologist.2014-0060

5. Prakash O, Lukiw WJ, Peruzzi F, et al. Gliomas and seizures. Medical Hypotheses. 2012; 79:622-626.

6. The Interphone Study Group. Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case–control study. Int J Epidemiol. 2010. 39: 675-94.

7. The INTERPHONE Study Group. Acoustic neuroma risk in relation to mobile telephone use: Results of the INTERPHONE international case-control study. Cancer Epidemiol 2011. 35:453-64.

8. Zhao H, Cai W, Su S et al. Allergic conditions reduce the risk of glioma: a meta-analysis based on 128,936 subjects. Tumor Biol. 2014. 35:3875-3880. https://10.1007/s13277-013-1514-4.

9. Ostrom QT, Fahmideh MA, Cote DJ, et al. Risk factors for childhood and adult primary brain tumors. Neuro-Oncology. 2019. 21:1357-1375. https://doi.org/10.1093/neuonc/noz123.

10. Buckingham SC, Robel S. Glutamate and tumor-associated epilepsy: Glial cell dysfunction in the peritumoral environment. Neurochem.Int. 2013. 63:696-701. https://dx.doi.org/10.1016/neuint.2013.01.027

Declarations

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Conflicts of interest

The authors confirm that they have no conflicts of interest.

Availability of data

Original data are not available as per ethical clearance and national data privacy legislations.

Code availability

Programming code of analysis used for the present paper can be obtained by contacting the corresponding author.

Authors' contributions

BS, MB and JS designed and jointly led the present project and drafted the manuscript. MM carried out the analysis. All other authors were also involved in the INTERPHONE study, its design, conduct and interpretation. EC was the overall coordinator of the INTERPHONE project. All authors reviewed and approved the manuscript.

Ethics approval

IARC Ethical approval was granted on 25 November 1999 (No ERC-Project 99-010). All study centers obtained national ethical approval.

Consent to participate

All participants of the INTERPHONE study filled in written informed consent.

Consent to publication

All authors critically reviewed and approved the final version of the manuscript.

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Table 1: Association between tumour and allergy or epilepsy, by time since start[1] and age at onset[2]

	Glioma		low grade glioma		high grade glioma		meningioma		acoustic neuroma	
	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)
Asthma										
Ever/never										
never	2453/2630	1.00	751/797	1.00	1678/1805	1.00	2161/2377	1.00	1001/1928	1.00
ever	220/303	0.73 (0.58-0.92)	82/107	0.89 (0.60-1.34)	137/196	0.65 (0.49-0.87)	228/263	0.91 (0.72-1.14)	99/204	1.02 (0.75-1.37)
Time since start										
never	2453/2630	1.00	751/797	1.00	1678/1805	1.00	2161/2377	1.00	1001/1928	1.00
< 10 years	49/92	0.67 (0.44-1.02)	25/29	1.05 (0.53-2.08)	23/63	0.47 (0.26-0.85)	66/73	0.91 (0.62-1.34)	34/70	0.99 (0.59-1.64)
10-19 years	37/60	0.53 (0.32-0.88)	18/25	0.80 (0.37-1.74)	19/35	0.36 (0.17-0.76)	54/51	1.18 (0.71-1.94)	13/32	0.62 (0.28-1.37)
20 + years	134/151	0.85 (0.63-1.15)	39/53	0.84 (0.48-1.49)	95/98	0.84 (0.59-1.21)	108/139	0.83 (0.61-1.13)	52/102	1.20 (0.80-1.80)
Age at onset										
never	2453/2630	1.00	751/797	1.00	1678/1805	1.00	2161/2377	1.00	1001/1928	1.00
child (0-9)	93/103	0.80 (0.56-1.15)	22/38	0.66 (0.33-1.30)	71/65	0.87 (0.57-1.33)	53/82	0.57 (0.36-0.89)	36/61	1.30 (0.79-2.15)
young (10-19)	39/43	0.95 (0.55-1.64)	17/20	0.83 (0.36-1.92)	22/23	1.09 (0.54-2.23)	39/33	1.37 (0.79-2.40)	15/30	1.29 (0.60-2.78)
adult (20+)	88/157	0.62 (0.45-0.86)	43/49	1.09 (0.64-1.86)	44/108	0.40 (0.26-0.63)	136/148	1.00 (0.75-1.33)	48/113	0.81 (0.54-1.23)
Hay Fever										
Ever/never										
never	2251/2365	1.00	684/713	1.00	1546/1628	1.00	2006/2162	1.00	895/1720	1.00
ever	410/558	0.72 (0.61-0.86)	150/194	0.86 (0.63-1.15)	256/360	0.67 (0.54-0.84)	370/465	0.91 (0.76-1.10)	201/402	0.91 (0.72-1.14)
Time since start										
never	2251/2365	1.00	684/713	1.00	1546/1628	1.00	2006/2162	1.00	895/1720	1.00
< 10 years	80/117	0.67 (0.47-0.96)	30/41	0.99 (0.57-1.73)	49/76	0.53 (0.33-0.85)	82/105	0.96 (0.66-1.40)	54/99	0.95 (0.61-1.48)
10 – 19 years	75/126	0.56 (0.39-0.79)	28/48	0.52 (0.27-0.99)	46/76	0.57 (0.36-0.89)	83/109	0.86 (0.61-1.21)	41/92	0.77 (0.49-1.22)
20 + years	255/315	0.81 (0.66-1.01)	92/105	0.95 (0.65-1.38)	161/208	0.77 (0.59-1.01)	205/251	0.92 (0.73-1.16)	106/211	0.95 (0.71-1.28)
Age at onset										
never	2251/2365	1.00	684/713	1.00	1546/1628	1.00	2006/2162	1.00	895/1720	1.00
child (0-9)	89/107	0.84 (0.59-1.21)	34/39	0.99 (0.55-1.78)	55/67	0.77 (0.48-1.24)	58/68	1.04 (0.68-1.58)	32/64	0.96 (0.58-1.59)

young (10-19)	131/174	0.75 (0.56-1.00)	51/69	0.80 (0.50-1.28)	79/103	0.77 (0.53-1.12)	106/128	0.85 (0.63-1.16)	59/122	0.95 (0.64-1.39)
adult (20+)	190/277	0.67 (0.53-0.84)	65/86	0.84 (0.55-1.28)	122/190	0.60 (0.45-0.80)	206/269	0.92 (0.72-1.16)	110/216	0.87 (0.64-1.18)
Eczema										
Ever/never										
never	2350/2491	1.00	723/762	1.00	1605/1707	1.00	2064/2207	1.00	954/1791	1.00
ever	313/435	0.78 (0.64-0.94)	110/145	0.73 (0.51-1.03)	200/284	0.78 (0.61-0.98)	316/426	0.84 (0.70-1.02)	145/333	1.02 (0.78-1.32)
Time since start										
never	2350/2491	1.00	723/762	1.00	1605/1707	1.00	2064/2207	1.00	954/1791	1.00
< 10 years	55/108	0.58 (0.39-0.85)	21/41	0.48 (0.25-0.92)	34/65	0.66 (0.40-1.08)	58/97	0.81 (0.55-1.21)	26/81	0.79 (0.46-1.37)
10 -19 years	69/83	0.91 (0.62-1.34)	24/23	0.79 (0.37-1.67)	43/59	0.87 (0.54-1.40)	66/73	1.03 (0.68-1.55)	32/70	1.09 (0.64-1.87)
20 + years	189/244	0.82 (0.65-1.05)	65/81	0.85 (0.56-1.31)	123/160	0.79 (0.59-1.07)	192/256	0.81 (0.64-1.02)	87/182	1.09 (0.79-1.51)
Age at onset										
never	2350/2491	1.00	723/762	1.00	1605/1707	1.00	2064/2207	1.00	954/1791	1.00
child (0-9)	93/125	0.75 (0.53-1.05)	35/51	0.75 (0.44-1.27)	57/70	0.76 (0.48-1.21)	89/108	0.81 (0.59-1.13)	44/92	0.93 (0.60-1.44)
young (10-19)	77/87	1.07 (0.74-1.54)	29/25	1.10 (0.55-2.19)	47/62	0.98 (0.63-1.55)	67/97	0.83 (0.57-1.21)	33/65	1.36 (0.80-2.31)
adult (20+)	143/223	0.68 (0.53-0.89)	46/69	0.57 (0.34-0.94)	96/152	0.70 (0.51-0.97)	160/221	0.87 (0.67-1.12)	68/176	0.96 (0.67-1.37)
Past/current										
never	2348/2485	1.00	722/761	1.00	1604/1702	1.00	2060/2200	1.00	954/1784	1.00
past	127/138	1.01 (0.74-1.37)	47/44	1.01 (0.58-1.77)	79/93	0.95 (0.65-1.39)	125/135	1.03 (0.75-1.40)	55/107	1.13 (0.73-1.74)
current	179/291	0.67 (0.53-0.85)	61/98	0.63 (0.42-0.95)	116/188	0.68 (0.51-0.91)	184/283	0.76 (0.60-0.95)	87/218	0.96 (0.71-1.32)
Allergies										
Any allergy										
none	1903/1894	1.00	568/565	1.00	1316/1309	1.00	1661/1731	1.00	757/1393	1.00
at least one	721/989	0.71 (0.61-0.82)	253/327	0.78 (0.60-1.01)	462/654	0.67 (0.56-0.80)	699/878	0.86 (0.74-1.00)	336/715	0.91 (0.75-1.11)
Time since start										
never	1903/1894	1.00	568/565	1.00	1316/1309	1.00	1661/1731	1.00	757/1393	1.00
< 10 years	126/229	0.56 (0.42-0.74)	47/74	0.68 (0.42-1.09)	78/154	0.50 (0.35-0.71)	135/189	0.77 (0.58-1.03)	81/178	0.85 (0.59-1.21)
10 – 19 years	137/196	0.65 (0.49-0.86)	51/68	0.63 (0.38-1.03)	83/126	0.61 (0.43-0.87)	144/177	0.84 (0.63-1.12)	65/145	0.81 (0.55-1.17)
20 + years	458/564	0.79 (0.66-0.94)	155/185	0.88 (0.65-1.20)	301/374	0.75 (0.61-0.93)	420/512	0.89 (0.75-1.06)	190/392	0.98 (0.77-1.24)
Age at onset										
never	1903/1894	1.00	568/565	1.00	1316/1309	1.00	1661/1731	1.00	757/1393	1.00

child (0-9)	215/281	0.71 (0.56-0.90)	72/104	0.77 (0.52-1.15)	142/172	0.69 (0.51-0.94)	171/209	0.83 (0.64-1.07)	87/177	0.95 (0.68-1.32)
young (10-19)	193/233	0.84 (0.65-1.07)	76/82	0.89 (0.57-1.38)	115/150	0.80 (0.59-1.10)	169/202	0.93 (0.72-1.20)	82/167	1.06 (0.75-1.49)
adult (20+)	313/475	0.65 (0.53-0.78)	105/141	0.73 (0.51-1.04)	205/332	0.60 (0.47-0.76)	359/467	0.84 (0.70-1.02)	167/371	0.83 (0.64-1.07)
Epilepsy										
Ever/never										
never	2499/2811	1.00	775/882	1.00	1701/1902	1.00	2276/2532	1.00	1061/2057	1.00
ever	101/33	2.94 (1.87-4.63)	48/10	5.71 (2.48-13.1)	52/23	2.01 (1.14-3.54)	61/32	2.12 (1.27-3.56)	17/26	1.44 (0.68-3.07)
Time since start										
never	2499/2811	1.00	775/882	1.00	1701/1902	1.00	2276/2532	1.00	1061/2057	1.00
< 10 years	52/7	8.44 (3.28-21.7)	25/2	21.7 (2.89-163)	26/5	5.09 (1.66-15.6)	21/5	6.73 (1.90-23.9)	1/8	0.16 (0.01-1.84)
10 – 19 years	21/4	3.62 (1.09-12.0)	14/3	3.64 (0.91-14.5)	7/1	3.38 (0.38-30.4)	12/2	4.37 (0.83-22.9)	5/2	15.7 (1.00-242)
20 + years	28/22	1.28 (0.67-2.46)	9/5	2.15 (0.50-9.23)	19/17	1.09 (0.51-2.32)	28/25	1.32 (0.71-2.43)	11/16	1.70 (0.68-4.28)
Age at onset										
never	2499/2811	1.00	775/882	1.00	1701/1902	1.00	2276/2532	1.00	1061/2057	1.00
child (0-9)	9/10	0.97 (0.31-2.99)	5/3	3.52 (0.33-37.8)	4/7	0.63 (0.16-2.45)	14/13	1.24 (0.51-3.02)	3/5	1.38 (0.32-6.02)
young (10-19)	15/11	0.94 (0.38-2.33)	7/3	1.72 (0.39-7.57)	8/8	0.61 (0.18-2.02)	10/5	1.52 (0.45-5.10)	6/8	2.66 (0.72-9.76)
adult (20+)	77/12	6.61 (3.30-13.2)	36/4	10.68 (3.15-36)	40/8	4.89 (2.07-11.6)	37/14	3.35 (1.58-7.10)	8/13	0.90 (0.27-2.98)

[1]Between first diagnosis by a physician and two years before tumour diagnosis (cases) or reference date (controls)

[2]Reference category (never): no diagnosis of disease up to two years before tumour diagnosis (cases) or reference date (controls); adjusted for education and time at interview; cases and controls answering "don't know" for a disease or having missing values in the adjustment variables were excluded from analyses

Table 2: Association between tumour and allergy or epilepsy, by gender[1]

	glioma - men		glioma - women		meningioma - men		meningioma - women		ac. neuroma - men		ac. neuroma - women	
	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)	cases/ contr.	OR (CI-95%)
Asthma												
never	1477/1590	1.00	976/1040	1.00	519/575	1.00	1642/1802	1.00	488/943	1.00	513/985	1.00
ever	127/165	0.75 (0.55-1.02)	93/138	0.71 (0.50-1.02)	45/52	1.00 (0.61-1.63)	183/211	0.88 (0.68-1.14)	47/87	1.02 (0.63-1.63)	52/117	0.95 (0.64-1.42)
Hay Fever												
never	1360/1428	1.00	891/937	1.00	483/533	1.00	1523/1629	1.00	440/843	1.00	455/877	1.00
ever	234/319	0.67 (0.53-0.85)	176/239	0.75 (0.58-0.98)	81/95	0.87 (0.58-1.31)	289/370	0.91 (0.74-1.12)	93/181	0.93 (0.65-1.32)	108/221	0.85 (0.62-1.16)
Eczema												
never	1446/1536	1.00	904/955	1.00	521/552	1.00	1543/1655	1.00	473/898	1.00	481/893	1.00
ever	150/214	0.74 (0.56-0.97)	163/221	0.80 (0.61-1.05)	44/78	0.59 (0.36-0.94)	272/348	0.91 (0.74-1.12)	62/129	1.01 (0.65-1.55)	83/204	1.04 (0.74-1.45)
Any allergy												
none	1174/1176	1.00	729/718	1.00	423/445	1.00	1238/1286	1.00	378/708	1.00	379/685	1.00
1 and more	400/549	0.66 (0.54-0.80)	321/440	0.75 (0.6-0.94)	137/177	0.77 (0.56-1.06)	562/701	0.88 (0.74-1.04)	153/309	0.93 (0.69-1.27)	183/406	0.87 (0.67-1.14)
Epilepsy												
never	1493/1675	1.00	1006/1136	1.00	530/603	1.00	1746/1929	1.00	514/989	1.00	547/1068	1.00
ever	62/20	3.71 (2.02-6.82)	39/13	2.37 (1.16-4.81)	20/5	5.46 (1.67-17.8)	41/27	1.55 (0.86-2.79)	8/11	2.23 (0.65-7.66)	9/15	1.26 (0.46-3.43)

[1]Reference category (never): no symptoms of disease up to two years before tumour diagnosis (cases) or reference date (controls); adjusted for education and time at interview; cases and controls answering "don't know" for a disease or had missing values in the adjustment variables were excluded from analyses

Supplementary table: Description of the study population for the analyses of allergic conditions and epilepsy. Interphone Study Group

	glioma cases		meningioma cases		acoustic neuroma cases		controls[1]	
	n	%	n	%	n	%	n	%
Status of interview								
total ascertained	4301	100	3115	100	1361	100	14354	100
not interviewed	1536	36	690	22	240	18	6696	47
interviewed	2765	64	2425	78	1121	82	7658	53
Reasons for exclusion								
not interviewed	1536	*100*	690	*100*	240	*100*	6696	*100*
refused self	*470*	*31*	*339*	*49*	*148*	*62*	*4303*	*64*
doctor refusal	*198*	*13*	*69*	*10*	*23*	*10*	*126*	*2*
dead or too ill	*637*	*42*	*66*	*10*	*5*	*2*	*49*	*1*
language problems	*34*	*2*	*50*	*7*	*12*	*5*	*133*	*2*
unable to trace	*157*	*10*	*137*	*20*	*46*	*19*	*1819*	*27*
other reasons	*40*	*3*	*29*	*4*	*6*	*3*	*266*	*4*
interviewed[2]	72		29		19		1337	

	glioma				meningioma				acoustic neuroma			
	cases		controls		cases		controls		cases		controls	
	n	%	n	%	n	%	n	%	n	%	n	%
inclusion in analyses	2693	*100*	2957	*100*	2396	*100*	2649	*100*	1102	*100*	2137	*100*
men	1614	*60*	1768	*60*	569	*24*	634	*24*	536	*49*	1032	*48*
women	1079	*40*	1189	*40*	1827	*76*	2015	*76*	566	*511*	1105	*52*
age at reference date												
< 30 years	0	*0*	16	*1*	0	*0*	7	*0*	0	*0*	8	*0*
30 - 39 years	634	*24*	685	*23*	315	*13*	335	*13*	240	*22*	438	*20*
40 - 49 years	838	*31*	923	*31*	800	*33*	879	*33*	362	*33*	718	*34*
50 - 59 years	1221	*45*	1284	*43*	1281	*54*	1397	*53*	500	*45*	949	*44*

> 59 years	0	*0*	49	*2*	0	*0*	31	*1*	0	*0*	24	*1*
highest education level												
univ/high level tech/ postgrad	1103	*41*	1225	*41*	847	*35*	978	*37*	465	*42*	931	*44*
comprehensive middle school [3]	380	*14*	519	*18*	403	*17*	554	*21*	117	*11*	226	*11*
vocational/upper secondary [3]	491	*18*	539	*18*	424	*18*	479	*18*	176	*16*	343	*16*
high school graduate/less [4]	719	*27*	674	*23*	722	*30*	638	*24*	344	*31*	637	*30*

[1] the same control could be matched to more than one case

[2] nonparticipating in analyses because of incomplete data, unmatched

[3] in Denmark, Finland, Germany, Italy, Norway, and Sweden

[4] in France, Germany, UK, Australia, Canada, Japan, and New Zealand