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Residential proximity to power lines and risk of brain tumor in th general population

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Highlights

- ELF-MF exposure was estimated from power line location.
- Exposure to power lines was assessed by a lifetime geographical index.

Outline

Highlights
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1. Introduction
2. Methods
3. Results
4. Discussion
Author’s contribution
Funding
Patient consent

- An increased risk of brain tumors was associated with living near power lines.

Abstract

The effect of ELF-MF on human health is still controversial, particularly as regards long-term health effects like cancer. The literature does suggest, however, that they could be involved in the occurrence of brain tumors, although results concerning residential exposure are scarce. Our objective was to investigate the association between residential proximity to power lines and brain tumors among adults in France by using a geographical information system.CERENAT is a population-based case-control study carried out in France in 2004–2006. We used geographical data sources on power line location to create exposure scores based on distance between residence and power lines, and on the number of lines near residences. Conditional logistic regression for matched sets was used to estimate Odds Ratios (ORs) and 95% confidence intervals (95%CI).We found significant associations between cumulated duration living at <50 m to high voltage lines and: i) all brain tumors (OR 2.94; 95%CI 1.28–6.75); ii) glioma (OR 4.96; 95%CI 1.56–15.77). Further investigations are needed, particularly to improve the quality and availability of geographical and technical data on power lines.

Keywords

ELF-MF; Geographic information system; Environmental exposure; Glioma; Meningioma

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1. Introduction

Ethics approval

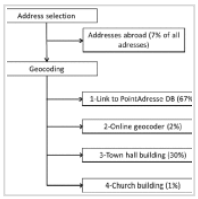
Declaration of competing ir

Acknowledgments

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Table 1. Description of stuc

Table 2. Description of ELF

Table 3. Description of ELF

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Due to the intense development of technologies using electricity over the last few decades, electromagnetic fields (EMF), including extremely low frequency electromagnetic fields (ELF-MF), are present in all living environments. Their effects on human health have been debated since the 1980's but remain controversial, particularly as regards long-term health effects like cancer, including brain tumors.

In 2002, ELF-MF were assessed as possibly carcinogenic to humans by the International Agency for Research on Cancer (Group 2B) mainly because of the association found with childhood leukemia but the evidence on brain tumor risk, both in adults and children, was limited (Gurney and van Wijngaarden, 1999), due to important methodological limits concerning exposure (IARC, 2002; SCENIHR. Health, 2009). Among the diverse sources of ELF-MF (electrical domestic appliances, specific occupational activities), the most studied when focusing on health effects are power lines. Associations in individuals living near power lines have not been found as clearly with other cancers (brain and breast tumors, malignant blood diseases) (ANSES, 2019), cardiovascular disease or reproductive disorders (Feychting, 2005).

In the past few decades, the incidence of primary brain tumors has increased in many countries such as Norway, Denmark, Finland, Sweden, France and the USA. This trend could be explained partly by the improvement of diagnosis techniques (Deltour et al., 2009; Helseth, 1995; Hoffman et al., 2006; Pouchieu et al., 2016). But temporal and spatial changes in the incidence of brain tumors also suggest the role of environmental factors, such as ionizing radiation (Umansky et al., 2008), and of other hypothetical environmental causes such as pesticides, solvents or metals (Wrensch et al., 2002).

Since the IARC classification in 2002 and a systematic review published in 2009 (SCENIHR. Health, 2009) sharing the same conclusion on the association of cancer and ELF-MF exposure, additional studies focused on adult brain tumors contributed to reinforce the evidence. A death certificate based case-control

study found an association between adult brain tumor mortality and living less than 50m from a power line (OR 1.10 95%CI 0.74–1.64) (Marcilio et al., 2011). A recent case-control study found an association between adult brain tumors and particularly meningioma and living less than 100m from a power line (OR 2.99, 95% CI 0.86–10.40) (Baldi et al., 2011).

A more recent case-control study also found an increased but not significant risk of adult brain tumors (OR 1.22; CI95% 0.88–1.69) among subjects living very near power lines (less than 50m) (Elliott et al., 2013). At last, a meta-analysis on ELF-MF and childhood brain tumors based on data from ten studies found a non-significant association (OR 1.14; 95% CI: 0.61, 2.13) for children exposed to more than 0.4μT in the home at diagnosis, the home at birth or the longest home (Kheifets et al., 2010). But there were many differences between the studies in the exposure assessment: long-term measurements, spot measurements or calculated fields. Furthermore, most of them did not consider histological subtypes of brain tumors.

Exposure to ELF-MF emitted by power lines can be assessed by two approaches: direct and indirect methods. The main direct method relies on ELF-MF measurements at a given location and over a given period of time, generally considered as being the most representative of actual exposure (Schoenfeld et al., 1999). Another available direct method is individual monitoring, involving the use of wearable dosimeters, and measuring individual ELF-MF exposures throughout the day (Schoenfeld et al., 1999; McBride et al., 1999; Eskelinen et al., 2002). These approaches take into account any exposure source without the ability to consider separately each and every one of them. Furthermore, both direct methods give information on current ELF-MF exposure only but no information on historical exposure.

Among the indirect methods, geographical information system (GIS)-based methods may be an effective tool, when paired with declarative data such as residential history, to assess residential ELF-MF exposure in the general population (Blaasaas and Tynes,

2002). It is a valuable alternative considering the difficulties in gathering historical data on ELF-MF measurements. Geographical indicators based on the location of power lines have been successfully used as surrogates for ELF-MF measurements. The most used indicator is the distance from the lines, according to the voltage, combined with levels of magnetic fields, and frequently expressed in thresholds of exposure in μT (Blaasaas and Tynes, 2002; Wartenberg et al., 1993; Kliukiene et al., 2004; Habermann et al., 2010). The geographical indicators can be associated or not with additional data on power line characteristics and they can help build algorithms usable in epidemiological studies, as has been done in several studies on childhood leukemia (Verkasalo et al., 1993; Malagoli et al., 2010; Sermage-Faure et al., 2013; Kheifets et al., 2015).

Historical exposure is very important, in order to identify etiological factors of brain tumors, because the latency between exposure to a carcinogenic factor and the occurrence of solid tumors may represent several decades. This is where indirect measurements (such as GIS methods) are highly needed.

The objective of our study was to investigate the association between residential proximity to power lines used as a proxy for ELF-MF exposure, and brain tumors among adults in France, using a geographical information system.

2. Methods

CERENAT is a multicentric population-based case-control study initiated in 2004, designed to study the role of occupational and environmental factors in the etiology of primary brain tumors in adults. The methods have been described in greater detail in a previous publication (Coureau et al., 2014).

2.1. Population

In brief, CERENAT cases were aged 16 years or over, had benign or malignant brain tumors diagnosed between June 2004 and May 2006, and were living in one of four French areas (Gironde,

Calvados, Manche, Hérault) at the time of diagnosis. These four areas were chosen because of the presence of a population-based cancer registry that helped to identify the patients. Patients were primarily identified, however, with the collaboration of a network of practitioners involved in the diagnosis and treatment of patients with brain tumors. All the diagnoses were confirmed by either a neuropathological assessment or for cases with no histological diagnosis, by clinical and iconography assessment.

Primary brain tumors with the following ICDO-3 topography codes were included: C70.0-C70.9, C71.0-C71.9 and C72.0-C72.9. Patients with recurrent tumors, metastases, pituitary tumor genetic syndrome or AIDS were excluded.

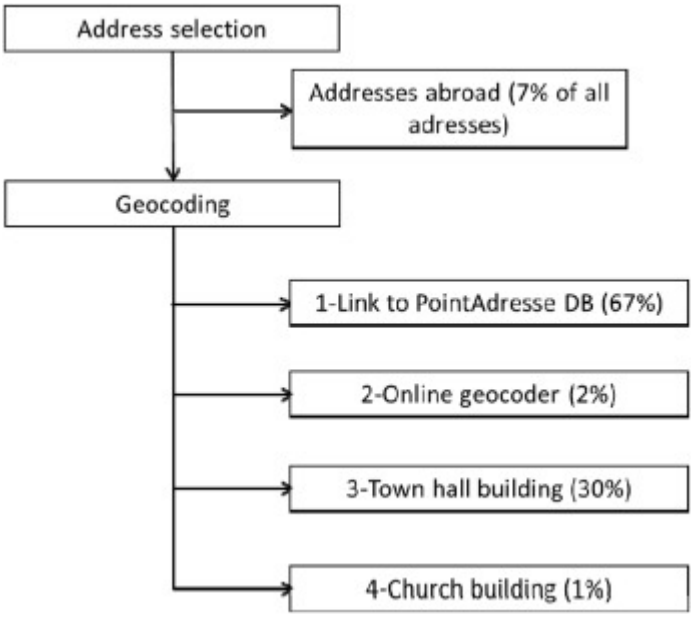
Cases were grouped according to morphology codes as gliomas, meningiomas, acoustic neuromas, lymphomas and other unspecified primary brain tumors (McCarthy and Kruchko, 2005). In this analysis, only cases with glioma and meningioma were considered. For each case, two controls with no history of brain tumors were randomly selected from the local electoral rolls during the period 2005–2008. They were matched individually on age (±2 years), gender and area of residence.

2.2. Data collection

Data were collected through standardized questionnaires delivered as face-to-face structured interviews. When cases were deceased or in a severe clinical condition, a relative was invited to complete a simplified questionnaire. Their matched controls completed the simplified questionnaire themselves. The questionnaire covered sociodemographic characteristics, medical history, lifestyle, detailed occupational and environmental data and lifetime residential history including all addresses from birth to the date of diagnosis, where the individual had been living for one year or more. For each address, street number, type and name, zip code, city, arrival and departure year were collected.

2.3. Residential exposure data

Addresses collected in the residential history of cases and controls and located in mainland France and Corsica (93% of collected addresses) were geocoded according to four steps (Fig. 1). The first step linked an address directly during input with a geographical database of all addresses in France (PointAdresse Database from the French National Geographical Institute V2.1) (67% of addresses) (Institut de l'InformationGéographiqueetforestière). If the address was not in PointAdress, we used an online geocoder, based on data from Google Maps (2% of addresses) (On line Geocoder. Availab). In the third and fourth steps, we used data from another geographical database containing public and administrative buildings, the BDTopo database V2.1, also from the French National Geographic Institute (Institut de l'InformationGéographiqueetforestière. Base de données BD TOPO), consisting in locating addresses which could not be geocoded by the previous methods: in the third step, at the municipality's town hall building center (30%) and, if that was not possible, in the fourth step, at the municipality's church center (1%). If more than one church existed in the municipality, we chose the church located in the most densely populated area. Addresses located abroad or in French Overseas Departments or Territories were not geocoded, for feasibility reasons (7% of collected addresses). Geo-positioning was carried out for all addresses, at least at the municipality level. Because no past or present data on ELF-MF measurements in the environment were available for the areas of the study, we decided to use residential proximity to high-voltage power lines as a proxy to estimate lifelong ELF-MF exposure, based on a database from the single French electricity distribution company ("Réseau de Transport d'Electricité", RTE) (http://www.rte-france.com, 2016), with the help of a GIS-based system. The RTE geographical database contains information on all power lines located in mainland France, overhead or underground, in 2013 (Fig. 2). Power lines were categorized according to their voltage:< 45 kV; 45 kV; 63 kV; 90 kV; 150 kV; 225 kV; 400 kV.



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Fig. 1. Address geocoding method. *(DB: database)*.



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Fig. 2. Map of power lines in Mainland France, RTE 2013.

2.4. Assessment of ELF-MF exposure

We chose to estimate ELF-MF exposure by a proxy such as residential proximity to power lines, from 1965 to 2006. We did not make a distinction between overhead and underground lines during the construction of the exposure indexes and we assumed that the French electricity network did not change between 1965 and 2013, the date of the RTE database.

If the address of the residence had not been collected or could not be geocoded, we considered that exposure to ELF-MF was null at this given address.

We created two different exposure scores using QGIS V2.14.3 geographical information system software (QGIS Development Team, 2009. Open Source Geospatial Foundation).

One metric was based on exposure corridors around the lines, representing a threshold for exposure to ELF-MF of approximatively 0.3 μT, and the other one was based on a distance threshold - between the residence and the nearest power line - that has been associated with brain tumors in previous studies (Marcilio et al., 2011; Elliott et al., 2013). For the score based on corridors, we defined thresholds for exposure, represented as buffers around the power lines, of approximatively 0.3 μT, according to data from the literature (Blaasaas and Tynes, 2002; Wartenberg et al., 1993; Kliukiene et al., 2004; Habermann et al., 2010; Kheifets et al., 2015) and adjusting to the voltage levels used in France. The thresholds defined in previous studies were calculated according to two different methods: i) by using statistical models taking account of power line characteristics (such as the height of electric towers, the average load or phase of the line) alone (Kliukiene et al., 2004), associated with measurements (Kheifets et al., 2015) or associated with data from the literature (Habermann et al., 2010); ii) by using data from the literature and from technical reports (Blaasaas and Tynes, 2002; Wartenberg et al., 1993).

According to the literature and for a threshold of 0.3 μT, the correspondences between voltage and distance were as follows: i) 63 kV: 60 m; ii) 90 kV: 80 m; iii) 150 kV: 100 m; iv) 225 kV: 150 m; and v) 400 kV: 200 m. Then, we calculated the number of power lines close enough for a residence to be in the exposure corridor. If the residence was not in a corridor, we considered that exposure to ELF-MF was null.

Finally, to take account of cumulated exposure in every residence inhabited by a subject during his life, we created an exposure corridor score by calculating cumulative duration living in 1, 2 and 3 or more exposure corridors for each subject during his lifetime.

For the score based on distance, we calculated the distance between the residence and: i) the nearest power line, ii) the nearest high voltage line (≤200 kV) and iii) the nearest very high voltage line (>200 kV). The threshold of 50 m was selected according to data from the literature (Marcilio et al., 2011; Elliott et al., 2013; Sermage-Faure et al., 2013). If the residence was at more than 50 m from a line, we considered that exposure to ELF-MF was null. Then, we created the distance exposure score by calculating cumulative duration of exposure (<50 m or not) during lifetime.

For both exposure metrics, the cumulative duration was defined as the sum of the durations living in a place of residence considered as exposed.

2.5. Potential confounders

The following potential confounders were considered: age, gender, level of education (primary or secondary school vs high school or university); smoking (pack-years), alcohol consumption (classified as high for men over three glasses per day, and over two glasses per day for women) and mobile phone use (cumulative call duration) (Coureau et al., 2014). Occupational exposure to pesticides was identified on the basis of detailed occupational histories and specific questionnaires on pesticide use, and was considered here as having performed treatment tasks (direct

exposure) on crops, gardens or wood, or as having been in contact (indirect exposure) with treated crops, wood or gardens in any job during their life. Household pesticide exposure in the CERENAT study was defined as having treated against crawling and flying insects at least once a week. Household exposure to ELF-MF was based on a specific questionnaire on the use of electrical appliances, on field measurements and on the literature. The electrical appliances studied in the CERENAT Study were: electric shaver, hair dryer, heating blanket, radio alarm, induction hob and hooded dryer. The data collected were the frequency of use (number of times per month) and the period of use in years. Field measurements (intensity in tesla and distance in meters from the source) were performed on these electrical appliances, when present in the homes of 14 staff members from the research team, as part of a pilot study. We used the literature to approximate the duration of use in minutes and when we had missing data from the other sources. Finally, we calculated a score by multiplying the duration of use, frequency of use, distance from the appliance, period of use and level of magnetic field emitted in μT.

2.6. Statistical analysis

The index date for each case and its two matched controls was the date of brain tumor diagnosis. ELF-MF residential exposure from power lines during the year before the index date was not taken into account, to consider a potential induction period and eliminate any reverse causality bias due to prodromal effects.

Missing dates in residential calendars were imputed when possible, considering the dates of previous and/or following residences.

Lifelong ELF-MF residential exposure from power lines was assessed with i) the cumulated and average duration living at less than 50 m from any line, HV and VHV lines and ii) the corridor exposure index. They were used as categorical indicators: binary (ever vs never exposure) and categorized on thresholds of duration based on literature (Huss et al., 2009): ≥5 years; ≥ 10

years; ≥15 years. The reference category consisted of subjects who had never been exposed at any time in their residential history.

Conditional logistic regressions for matched sets were used to estimate ORs and 95% CIs. All statistical tests were two-sided. Confounders were selected using the suitable selection algorithm (Bursac et al., 2008). Each exposure score was analyzed separately and adjusted for confounders. Five sensitivity analyses were performed: i) excluding participants who had at least one address in their residential history that could not be geocoded (foreign address (7%) or missing dates (0.6%)), and who were considered unexposed at that address in the main analysis, ii) excluding addresses that were imprecisely geocoded (i.e. at the municipality level), iii) considering a longer lag prior to the index date (2 and 5 years), iv) considering exposure misclassification bias using the method described by Lash et al. (2014), and v) calculating residential exposure metrics without imputing missing residential dates.

Analyses were performed using SAS, V9.3 software (SAS Institute, Cary, North Carolina, USA).

Table 1. Description of study population. CERENAT, 2004–2006, France.

	All brain tumors		
	N*	Cases (n=490)	Controls (n=98
		n (%)	n (%)
Age at diagnosis (mean±SD)	1470	57.6±14.4	57.5±14.2
Gender	1470		
Men		211 (43.1)	422 (43.1)
Women		279 (56.9)	558 (56.9)
Simplified questionnaire (Yes)	1470	75 (15.3)	150 (15.3)
Education Level	1469		
Primary or Secondary		306 (62.6)	505 (51.5)

	All brain tumors		
	N*	Cases (n=490)	Controls (n=98
		n (%)	n (%)
High school or University		183 (37.4)	475 (48.5)
Tobacco smoking (in pack-years)	1460		
0		229 (47.1)	486 (49.9)
]0–10[		94 (19.3)	195 (20.0)
]10–20[		56 (11.5)	121 (12.4)
≥20		107 (22.0)	172 (17.7)
Alcohol consumption at least once a week	1245		
No		209 (50.4)	268 (32.3)
Moderate		172 (41.5)	456 (54.9)
Excessive		34 (8.2)	106 (12.8)
Household exposure to ELF-MF	1470		
No		42 (8.6)	69 (7.0)
Yes		448 (91.4)	911(93.0)
Household exposure to pesticides	1449		
No		426 (89.5)	915 (94.0)
Yes		50 (10.5)	58 (6.0)
Occupational exposure to pesticides	1470		
No		293 (59.8)	506 (51.6)
Direct exposure		54 (11.0)	80 (8.2)
Indirect exposure		143 (29.2)	394 (40.2)
Self-reported cell phone use	1402		
Not user		246 (53.6)	481 (51.0)

	All brain tumors		
	N*	Cases (n=490)	Controls (n=98
		n (%)	n (%)
Cumulated duration of calls <896h		173 (37.7)	419 (44.4)
Cumulated duration of calls ≥896h		40 (8.7)	43 (4.6)

ELF-MF: extremely low frequency electromagnetic field.

3. Results

3.1. Population characteristics (Table 1)

Among the subjects defined as eligible, 95% of cases and 61% of controls could be reached, and a total of 596 (73%) cases and 1192 (45%) controls were included in the CERENAT study (Coureau et al., 2014). The participation rate was 66% for glioma and 75% for meningioma cases. The main reasons for non-participation of cases were refusals (48%), severe condition or death without proxy (38%) or unreachable subjects (14%). Non-included cases were older than included cases (mean age: 63 vs 58 years). After exclusion of acoustic neuromas (n=42), lymphomas and unspecified brain tumors (n=56), medullar tumors (n=50) and persons with missing residential history (2 meningioma cases and the four corresponding controls), 1470 subjects were included in the analysis: 273 cases and 546 controls for gliomas; 217 cases and 434 controls for meningioma. For gliomas and meningioma, neuropathological assessment represented 96% of diagnoses and clinical and radiological assessment 4%.

The median time between the index date and interview was 6 months (IQR: 4, 10) for cases and 21 months (IQR: 16, 29) for controls, and was similar for gliomas and meningiomas. Data was collected from relatives for 23% of gliomas and 6% of meningiomas. The average age at diagnosis was 55 years for gliomas and 60 years for meningiomas, and women represented

respectively 42% and 76% of the subjects (Table 1). The level of education was higher in controls than in cases ($p<10^{-3}$) as was the indirect occupational exposure to pesticides ($p<10^{-3}$). On the contrary, the alcohol consumption, the household exposure to pesticides and the cellphone use were higher in cases than in controls. There was no difference between cases and controls concerning the tobacco smoking and the household exposure to ELF-MF. Among the 1470 subjects, 300 (20%) had at least one address that could not be geocoded in their residential history but 67% of these addresses were inhabited before 1965 and therefore were not concerned by ELF-MF exposure assessment.

Table 2. Description of ELF-MF residential exposure from electric lines by address. CERENAT, 2004–2006, France.

	Adresses for All brain tumors		
	Total (n=6821)	**Cases (n=2281)**	**Cor**
	N (%)	**n (%)**	**n (%**
Exposure to all power lines			
Yes	227 (3.3)	75 (3.3)	152
1 line	154 (2.3)	49 (2.2)	105
2 lines	47 (0.7)	21 (0.9)	26 (
≥3 lines	26 (0.4)	5 (0.2)	21 (
Exposure to 63 kV power lines			
Yes	73 (1.1)	29 (1.3)	44 (
1 line	60 (0.9)	24 (1.1)	36 (
2 lines	7 (0.1)	4 (0.2)	3 (0
≥3 lines	6 (0.1)	1 (0.0)	5 (0
Exposure to 90 kV power lines			
Yes	12 (0.2)	6 (0.3)	6 (0
1 line	10 (0.2)	6 (0.3)	4 (0

	Adresses for All brain tumors		
	Total (n=6821)	**Cases (n=2281)**	**Cor**
	N (%)	**n (%)**	**n (%**
2 lines	2 (0.0)	0 (0.0)	2 (0
Exposure to 150 kV power lines			
Yes	0 (0.0)	0 (0.0)	0 (0
Exposure to 225 kV power lines			
Yes	146 (2.1)	43 (1.9)	103
1 line	96 (1.4)	27 (1.2)	69 (
2 lines	30 (0.4)	12 (0.5)	18 (
≥3 lines	20 (0.2)	4 (0.2)	16 (
Exposure to 400 kV power lines			
Yes	7 (0.1)	2 (0.1)	5 (0
1 line	7 (0.1)	2 (0.1)	5 (0
Addresses at the time of diagnosis	**n=1470**	**n=490**	**n=9**
Distance between all lines and residence			
>200 m	1395 (94.9)	465 (94.9)	930
50–200 m	60 (4.1)	20 (4.1)	40 (
<50 m	15 (1.0)	5 (1.0)	10 (
Distance between HV line and residence			
>200 m	1413 (96.1)	473 (96.5)	940
50–200 m	47 (3.2)	14 (2.9)	33 (
<50 m	10 (0.7)	3 (0.6)	7 (0
Distance between VHV line and residence			

	Adresses for All brain tumors		
	Total (n=6821)	Cases (n=2281)	Cor
	N (%)	n (%)	n (%
>200m	1447 (98.4)	479 (97.8)	968
50–200m	18 (1.2)	9 (1.8)	9 ((
<50m	5 (0.3)	2 (0.4)	3 ((

kV: kilovolt; HV: high voltage (<200kV); VHV: very high voltage (≥200kV).

3.2. ELF-MF exposure characteristics

3.2.1. ELF-MF exposure by address (Table 2)

When considering the 6821 addresses assessed for exposure to power lines, only 227 (3%) were in the exposure corridor of a power line and less than 1% were exposed to more than one power line with a maximum of 6 lines concerning 1 address and 225kV lines. These results did not differ between cases and controls. No address was exposed to 150kV lines. Exposure according to voltage was first to 225kV lines with 146 addresses (2%), then to 63kV lines (73 addresses, 1%). The other lines concerned less than 1% of the addresses.

The distance exposure indexes concerned the 1470 addresses inhabited at the time of diagnosis and 15 of them (1%) were located less than 50m from a power line whereas 1395 (95%) were located at a distance of more than 200m. Results were similar for cases and controls.

Table 3. Description of ELF-MF residential exposure from electric lines by subject. CERENAT, 2004–2006, France.

	All brain tumors (n=1470)		
	Cases (n=490)	Controls (n=980)	p-valu
	n (%)	n (%)	
Exposure to all power lines			0.481
Yes	60 (12.2)	128 (13.1)	
1 line	37 (7.6)	85 (8.7)	
2 lines	18 (3.7)	24 (2.5)	
≥3 lines	5 (1.0)	19 (1.9)	
Exposure to 63 kV power lines			0.305
Yes	26 (5.3)	41 (4.2)	
1 line	21 (4.3)	33 (3.4)	
2 lines	4 (0.8)	3 (0.3)	
≥3 lines	1 (0.2)	5 (0.5)	
Exposure to 90 kV power lines			–
Yes	6 (1.2)	6 (0.6)	
1 line	6 (1.2)	4 (0.4)	
2 lines	0 (0.0)	2 (0.2)	
Exposure to 150 kV power lines			–
Yes	0 (0.0)	0 (0.0)	
Exposure to 225 kV power lines			0.267
Yes	35 (7.2)	90 (9.2)	
1 line	19 (3.9)	59 (6.0)	
2 lines	12 (2.5)	16 (1.6)	
≥3 lines	4 (0.8)	15 (1.5)	
Exposure to 400 kV power lines			0.789
Yes	2 (0.4)	5 (0.5)	
1 line	2 (0.4)	5 (0.5)	

	All brain tumors (n=1470)		
	Cases (n=490)	Controls (n=980)	p-
	n (%)	n (%)	
Cumulative duration living <50m from any line			0.
Ever	30 (6.1)	46 (4.7)	
>5 years	18 (3.7)	20 (2.0)	
>10 years	9 (1.8)	12 (1.2)	
>15 years	8 (1.6)	8 (0.8)	
Cumulative duration living <50m from HV line			0.
Ever	19 (3.9)	19 (1.9)	
>5 years	11 (2.2)	11 (1.1)	
>10 years	4 (0.8)	7 (0.7)	
>15 years	4 (0.8)	6 (0.6)	
Cumulative duration living <50m from VHV line			0.
Ever	13 (2.7)	28 (2.9)	
>5 years	6 (1.2)	9 (0.9)	
>10 years	5 (1.2)	5 (0.5)	
>15 years	4 (0.8)	2 (0.2)	

	All brain tumors (n=1470)		
	Cases (n=490)	Controls (n=980)	p-
	n (%)	n (%)	
Cumulative duration living in at least 1 exposure corridor			0.
Ever	60 (12.2)	128 (13.1)	
>5 years	36 (7.4)	66 (6.7)	

	All brain tumors (n=1470)		
	Cases (n=490)	Controls (n=980)	p-
	n (%)	n (%)	
>10 years	20 (4.1)	44 (4.5)	
>15 years	17 (3.5)	28 (2.9)	
Cumulative duration living in 1 exposure corridor			0.
Ever	43 (8.8)	90 (9.2)	
>5 years	26 (5.3)	51 (5.2)	
>10 years	16 (3.3)	32 (3.3)	
>15 years	14 (2.9)	23 (2.4)	
Cumulative duration living in 2 exposure corridors			0.
Ever	19 (3.9)	25 (2.6)	
>5 years	8 (1.6)	10 (1.02)	
>10 years	2 (0.4)	4 (0.4)	
>15 years	1 (0.2)	1 (0.1)	
Cumulative duration living in 3 exposure corridors			0.
Ever	5 (1.0)	19 (1.9)	
>5 years	1 (0.2)	9 (0.9)	
>10 years	1 (0.2)	4 (0.4)	
>15 years	0 (0.0)	2 (0.2)	

HV: high voltage (<200kV); VHV: very high voltage (≥200kV).

3.2.2. ELF-MF exposure by subject (Table 3)

Among the 1470 subjects, 122 (8%) had lived at least once between 1965 and the time of diagnosis in a residence located in the exposure corridor of one power line and 66 (4%) in the exposure corridor of more than one line with a maximum of 6 lines concerning one subject (0.2%). As for the addresses, 225 kV lines were the most concerned with 125 (9%) subjects exposed and no one was ever exposed to 150 kV lines. Results were similar for cases and controls.

When considering the distance exposure indexes, 1% of the subjects had lived at the time of diagnosis less than 50 m from a power line (1% for high voltage lines and 0.2% for very high voltage lines) while 93% of the subjects never lived less than 200 m of any power line (95% for high voltage and 98% for very high voltage). These results did not change between cases and controls.

Among the 1470 subjects, 76 (5.2%) ever lived at less than 50 m from a power line, only 28 (1.9%)≥5 years, 21 (1.4%)≥10 years and 16 (1.1%)≥15 years during lifetime.

3.3. Multivariate analysis

Table 4 presents the adjusted risks concerning all brain tumors, gliomas and meningiomas associated with cumulative duration at less than 50 m from power lines and living in exposure corridors.

Table 4. Adjusted conditional logistic regression for ELF-MF residential exposure from electric lines. CERENAT, 2004–2006, France.

	All brain tumors				**Gliomas**
	Ca (n=389)	**Co (n=795)**	**OR [95% CI]**	**p-value**	**Ca (n=19**
Cumulative duration living <50m from any line					
Never	349	750	Reference		172
Ever	27	38	1.77 [0.98–3.20]	0.060	17
>5 years	15	18	2.09 [0.94–4.61]	0.069	6
>10 years	8	10	2.03 [0.69–5.97]	0.197	1

	All brain tumors				Gliomas
	Ca (n=389)	Co (n=795)	OR [95% CI]	p-value	Ca (n=196
>15 years	7	6	4.33 [1.11–16.9]	0.035	1
Cumulative duration living <50m from HV line					
Never	359	774	Reference		178
Ever	17	14	2.94 [1.28–6.75]	0.011	11
>5 years	9	9	2.56 [0.85–7.75]	0.096	3
>10 years	4	5	2.02 [0.39–10.63]	0.406	0
>15 years	4	4	3.92 [0.64–24.05]	0.140	0
Cumulative duration living <50m from VHV line					
Never	364	764	Reference		181
Ever	12	24	1.22 [0.57–2.61]	0.616	8
>5 years	5	9	1.35 [0.42–4.34]	0.615	2
>10 years	4	5	2.03 [0.50–8.31]	0.326	1
>15 years	3	2	4.70 [0.63–35.1]	0.131	1

	All brain tumors				Gliomas
	Ca (n=389)	Co (n=795)	OR [95% CI]	p-value	Ca (n=196
Cumulative duration living in at least 1 exposure corridor					
Never	327	680	Reference		162
Ever	49	108	0.92 [0.61–1.38]	0.675	27
>5 years	31	59	1.04 [0.64–1.71]	0.872	13
>10 years	19	38	0.97 [0.53–1.79]	0.921	8
>15 years	16	24	1.33 [0.66–2.70]	0.427	7
Cumulative duration living in 1 exposure corridor					
Never	340	713	Reference		170
Ever	36	75	0.90 [0.56–1.44]	0.655	19
>5 years	23	46	0.92 [0.52–1.63]	0.771	8

	All brain tumors				Gliomas
	Ca (n=389)	Co (n=795)	OR [95% CI]	p-value	Ca (n=196
>10 years	15	28	1.01 [0.50–2.04]	0.990	6
>15 years	13	19	1.30 [0.58–2.89]	0.527	6
Cumulative duration living in 2 exposure corridors					
Never	361	766	Reference		179
Ever	15	22	1.53 [0.73–3.20]	0.256	10
>5 years	6	9	1.34 [0.43–4.20]	0.620	4
>10 years	2	4	1.71 [0.25–11.81]	0.588	1
>15 years	1	1	2.69 [0.15–49.43]	0.505	0
Cumulative duration living in 3 exposure corridors					
Never	371	772	Reference		186
Ever	5	16	0.87 [0.27–2.83]	0.813	3
>5 years	1	8	0.29 [0.03–2.62]	0.269	0
>10 years	1	3	0.69 [0.07–6.85]	0.751	0
>15 years	0	2	–	–	0

*Data available for analysis; ¥ p value for global test; HV: high voltage (<200kV); VHV: very high voltage (≥200kV); £ OR for each indicator adjusted for gender, age, education level, tobacco and alcohol consumption, occupational and household exposure to pesticides, household exposure to ELF-MF and mobile phone use.

3.3.1. All brain tumors (Table 4)

Concerning the cumulative duration at less than 50m from any power line, a significant association was observed with brain tumors for people exposed for 15 years (OR 4.33, 95%CI 1.11–16.9), but not for people ever exposed or exposed for 5 and 10 years.

For the cumulative duration at less than 50m from high voltage power lines, a significant association with brain tumors was found for ever/never exposure (OR 2.94, 95%CI 1.28–6.75), but not for people exposed for 5, 10 or 15 years.

For the cumulative duration at less than 50m from very high voltage lines, no association was observed.

Concerning cumulative duration in exposure corridors, no association was observed with brain tumors, regardless of the number of corridors and the type of exposure.

Sensitivity analyses (excluding subjects with non-geocoded addresses; excluding addresses geocoded at the municipality level; with a 2-year and a 5-year exposure lag; considering exposure misclassification bias; with no imputation of residence dates), reported no difference in the observed associations (data not shown).

3.3.2. Gliomas (Table 4)

For the cumulative duration at less than 50m from any power line, a significant association with gliomas was observed for ever/never exposure (OR 3.23 95%CI 1.33–7.82), but not for people exposed for 5, 10 and 15 years.

For the cumulative duration at less than 50m from high voltage power lines, a significant association with gliomas was also observed for ever/never exposure (OR 4.96 95%CI 1.56–15.77), but not for people exposed for 5, 10 and 15 years.

Concerning the cumulative duration at less than 50m from very high voltage lines, no association was observed with gliomas, for ever/never exposure or for people exposed for 5, 10 and 15 years.

Concerning cumulative duration in exposure corridors, no association was observed with gliomas, regardless of the number of corridors and the type of exposure.

Sensitivity analyses (excluding subjects with non-geocoded addresses; excluding addresses geocoded at the municipality

level; with a 2-year and a 5-year exposure lag; considering exposure misclassification bias; with no imputation of residence dates) reported no difference in the observed associations (data not shown).

3.3.3. Meningiomas (Table 4)

No association was observed between meningiomas and proximity to power lines, except for the cumulative duration at less than 50m from any power line, with a significant association for people exposed for 15 years (OR 8.53; 95%CI 1.48–49.17). Furthermore, ORs appear to increase with duration, for cumulative duration at less than 50m but not for duration in exposure corridors.

Sensitivity analyses (excluding subjects with non-geocoded addresses; excluding addresses geocoded at the municipality level with a 2-year and a 5-year exposure lag; considering exposure misclassification bias; with no imputation of residence dates) reported no difference in the observed associations (data not shown).

4. Discussion

The objective of this study was fulfilled by analyzing the association between brain tumors and exposure to ELF-MF by two geographical methods including the use of the distance between the residence and the power lines and the use of exposure corridors according to the voltage. We observed some significant positive associations between cumulative duration at less than 50m to any line for exposure above 15 years and brain tumors (OR 4.33, 95%CI 1.11–16.9) and meningioma (OR 8.53, 95%CI 1.48–49.17). Gliomas were also significantly associated with cumulative duration at less than 50m but only for ever/never exposure to any line (OR 3.23, 95%CI 1.33–7.82) and high voltage lines (OR 4.96, 95%CI 1.56–15.77). No association was found between brain tumors, gliomas or meningiomas and cumulative duration in exposure corridors.

We observed significant association for the highest exposure to cumulative duration at less than 50m to any line and high voltage lines but not for very high voltage lines, which is surprising because very high voltage lines should emit more ELF-MF than lines with a lower voltage. But very high voltage lines are more often built in rural areas with low density of population and are used to transport power, not to deliver it and are often very high, up to 100m high. Therefore, residences near very high voltage lines may be farthest from the lines than residences near high voltage lines.

We did not find any significant association for cumulative duration in exposure corridors, whereas we could expect that exposure at less than 50m and exposure in corridors should be similar. But the threshold of 0.3μT corresponded to a distance of more than 50m, and until 400m for 400kV lines and could be improved. Moreover, we had in our study, globally, a very low number of subjects highly exposed to ELF-MF, probably leading to a lack of statistical power.

Exposure metrics based on proximity to power lines have already been used to assess residential ELF-MF exposure (Verkasalo et al., 1993; Malagoli et al., 2010; Sermage-Faure et al., 2013; Kheifets et al., 2015) and could prove to be better estimates than scores based on self-reported data. In this study, we did not pair our exposure scores with algorithms because of a lack of data, but score results based on the location of power lines were consistent with field measurements in the literature (Blaasaas and Tynes, 2002).

We chose to use two kinds of exposure scores: one based on exposure corridors around the lines and the other based on the distance between residences and power lines. Exposure corridors, corresponding to a threshold of 0.3μT, were designed as buffers around the lines and their radius depended on the voltage. The corridors were defined according to data from publications having used similar exposure scores (Blaasaas and Tynes, 2002; Wartenberg et al., 1993; Kliukiene et al., 2004; Habermann et al., 2010; Kheifets et al., 2015). This exposure score allowed simultaneous exposure to several power lines to be taken into

account. The exposure score based on distance took account only of the nearest line, but when power lines are close or cross, ELF-MF may partially cancel or add up, depending on several parameters such as the position of the lines, phase and intensity. Furthermore, even if the score based on distance did not take precise account of the voltage, exposure to high voltage (<200kV) and very high voltage (≥200kV) lines was estimated separately.

The CERENAT multicentric study was conducted on the general population and covered various socioeconomic statuses and environmental exposures. Cases were included from a clinical network supported by population-based cancer registries, thus ensuring the reliability of diagnosis. Controls were selected randomly from the electoral rolls, which include 90% of people above 18 years and are representative of the French general population in terms of age and gender (Pan Ké Shon, 2004). The delay between index date and interview was longer for controls, but we censured information on ELF-MF exposure one year before the index date. A large amount of data was collected through face-to-face interviews, such as adjustment variables and complete residential history. The availability of individual adjustment factors in a study on residential or geographical exposure to power lines is a strength, particularly when compared with ecological studies. Ecological studies usually use aggregated data on potential confounders and could therefore lead to a lack of precision in the estimation of the associations. The availability of complete and detailed residential history for all participants is another strength of our study. We could estimate exposure for all residences occupied by a participant in mainland France during their lifetime.

The chosen exposure metrics were based on one geographical data source, built for another purpose than epidemiology. Data from the electricity distribution company (RTE) was initially created to manage the transport and distribution of electricity and was not planned to be used to assess environmental exposure. However, the use of this source, with its advantages and limits, could show

how to define the necessary parameters for a more appropriate exposure source.

We did not differentiate underground and overhead lines in our analysis, as this information was not often defined in the literature. One publication considered that ELF-MF emitted by underground lines were much lower than ELF-MF emitted by overhead lines, which could lead to an overestimation of exposure (Pedersen et al., 2014). However, 86% of the power lines in the RTE database are overhead, so the impact on the exposure estimation should be limited.

Other methods were used in the literature to estimate ELF-MF exposure emitted by power lines, and particularly mathematical modeling of magnetic flux density. These calculations needed numerous power line characteristics such as the power, annual charge, location of electric conductors on the line and phase (Verkasalo et al., 1993; Kheifets et al., 2015; Olsen et al., 1993). These characteristics were not available in the RTE database.

Another limitation of the exposure scores is the inability to take account of factors that could modify the electrical power, such as seasons (more electrical use in winter) (Valjus et al., 1995). This could lead to errors in the estimation of exposure.

We defined one exposure time period from 1965 to the time of diagnosis of the case, based on the available version of RTE data and considered that the electricity network did not change during this period. Therefore, the exposure scores designed here possibly overestimated ELF-MF exposure because it took account only of the electricity network in 2013 yet the French electricity network has increased greatly since its beginnings and more particularly since the 1960s. In order to assess exposure misclassification from the lack of historical data on power lines, sensitivity analysis were conducted, using the method described by Lash et al. (2014) and it did not change the associations.

On the other hand, we considered that the latency of exposure of 40 years was sufficient to show an association between ELF-MF

exposure and the risk of brain tumor, although no accurate number for this latency is defined in the literature.

The exposure metrics were based on self-reported residential history covering the time period from birth to the time of study, which could lead to a misclassification of exposure, particularly for older addresses. But self-reported residential history has been considered reliable in literature (Künzli et al., 1996), and having all addresses from birth to the time of diagnosis to assess ELF-MF exposure, and not just the last residence, is an actual strength in this study.

All addresses located on the mainland could be geocoded, even the oldest. Not all addresses were geocoded with a comparable precision, however, since some addresses were geocoded at the accurate location and others were located at the center of the municipality. In order to take account of this lack of precision, we performed a sensitivity analysis by excluding the addresses geocoded at the municipality level and it did not change the associations.

Our main results are consistent with previous studies on environmental exposure to ELF-MF and brain tumors (Marcilio et al., 2011; Baldi et al., 2011; Elliott et al., 2013) although the risk levels found in our study are higher.

The first study was a case-control study of brain tumors in adults assessing residential exposure to ELF-MF by using a single buffer of 100m around power lines, regardless of the voltage (Baldi et al., 2011), and found an increased risk for meningioma and not for glioma when living near power lines (OR 2.99 95%CI 0.86–10.40). The second publication, an historical case-control study based on death certificates, used a similar approach with a GIS-based exposure assessment and found a non-significant and weak association between brain tumor mortality and living near a power line (<50m) at the time of death (OR 1.10 95%CI 0.74–1.64) (Marcilio et al., 2011). The third publication was also a case-control study, based on data from a national cancer registry and focused on several adult cancers (Elliott et al., 2013). The authors

found no clear trend of increased risk associated with distance to power lines but an increased yet non-significant risk of brain tumors for distances closest to power lines (OR 1.22 95%CI 0.88–1.69). At last, a meta-analysis focused this time on occupational exposure and brain tumors in adults found a moderate excess of risk (14% for all brain tumors and 18% for glioma), for higher ELF-MF exposure (Kheifets et al., 2008), but there was heterogeneity in the exposure assessment between studies.

However, the publications in the literature are insufficiently conclusive, mainly because they focused on different types of tumors or assessed ELF-MF exposure in different ways.

Despite this study's limitations, our results strongly suggest that the risk of brain tumor, and particularly gliomas could be associated with residential ELF-MF exposure estimated by proximity of power lines, as several previous studies have already pointed out. This study demonstrates how public cartographic data can be used in epidemiological studies to estimate residential exposure, even if they were not designed for this purpose. The limitations resulting from the original purpose of these data could be overcome by combination with other data sources, such as power line characteristics or metrology to enhance exposure assessment accuracy.

Author’s contribution

CC elaborated the study design, created the exposure metrics, did the analysis and wrote the manuscript IB, PL, PF were major contributors in the development of the study design, the recruitment of patients and the data collection of the case-control study.IB supervised all the work All authors read and approved the final manuscript.

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Patient consent

Obtained.

Ethics approval

Comité consultatif sur le traitement de l'information en matière de recherché dans le domaine de la santé (CCTIRS); Comités consultatifs de Protection des Personnes dans la Recherche Biomédicale (CCPPRB); Commission Nationale de l'Informatique et des Libertés (CNIL).

Declaration of competing interest

The authors declare no conflict of interest.

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> …Estimated ORs were 0.95 (95% CI 0.59–1.56) and 1.25 (95% CI 0.93–1.61), respectively at these two exposure levels. Studies of the effects of exposure on risk of adult brain tumours are mixed, with a meta-analysis of occupational studies reporting an 18% increase in the risk of glioma for higher ELF exposure levels (Kheifets e 2008), with no clear pattern of risk, and conflicting results in relation to residential ELF exposure (Baldi et al., 2011; Carles et al., 2020; Elliott et al., 2013; Khan et al., 2021; Marcilio et al., 2011). With the considerable incr in use in children and adolescents in the last 15 years, an important question is the possible effect of mobile phones on BTs in young people.…

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