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ORIGINAL PAPER

Maternal occupational exposure to extremely low frequency magnetic fields and the risk of brain cancer in the offspring

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Abstract
Objectives To examine the contribution of maternal occupational exposure to extremely low frequency magnetic fields (ELF-MF) shortly before and during pregnancy on the incidence of childhood brain tumors.
Methods A total of 548 incident cases and 760 healthy controls recruited between 1980 and 2002 from two Canadian provinces (Québec and Ontario) were included in this study, and their mothers were interviewed. Quantitative occupational ELF-MF exposure in microTesla units was estimated using individual exposure estimations or a job exposure matrix. We used three metrics to analyze exposure: cumulative, average, and maximum level attained.
Results Using the average exposure metric measured before conception, an increased risk was observed for astroglial tumors (OR = 1.5, 95% CI = 1.0–2.4). During the entire pregnancy period, a significantly increased risk was observed for astroglial tumors as well as for all childhood brain tumors with the average metric (OR = 1.6, 95% CI = 1.1–2.5 and OR = 1.5, 95% CI = 1.1–2.2, respectively). Based on job titles, a twofold risk increase was observed for astroglial tumors (OR = 2.3, 95% CI = 0.8–6.3) and for all childhood brain tumors (OR = 2.3, 95% CI = 1.0–5.4) among sewing machine operators.
Conclusions Results are suggestive of a possible association between maternal occupational ELF-MF exposure and certain brain tumors in their offspring.

Keywords Brain neoplasms · Childhood neoplasms · Occupational exposure · Maternal exposure · Electromagnetic fields

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Introduction

The causes of childhood brain tumors are essentially unknown. Exposure to extremely low frequency magnetic fields (ELF-MF) (3–3,000 Hz) in North America is ubiquitous because of the many sources (e.g., computers, household appliances, and electric power lines) that are powered by 60-Hz fields. Associations between exposure to ELF-MF and certain adulthood cancers, particularly acute leukemia and brain tumors, have been suggested in some studies [1, 2]. In addition, several studies have been conducted on the association between residential ELF-MF exposure and childhood brain tumors; based on a recent meta-analysis of 13 epidemiologic studies, there was a consistent finding of a moderately increased risk of childhood brain tumors with residential exposure to magnetic fields above 0.3 or 0.4 microTesla (μT) [3]. However, the available findings for an association between childhood brain tumors and parental occupational ELF-MF exposure are inconsistent across studies [4–7]. The potential biological mechanism through which ELF-MF may cause carcinogenic effects has not yet been identified. However, one possible hypothesis has been proposed whereby ELF-MF may cause cancers by affecting the recombination probability of radical pairs and therefore influence the level of free radicals [8].

Compared with residential exposure, occupational environments present a greater opportunity for ELF-MF exposure, and, in some cases, a higher exposure level, such as in the electric utility industry [9]. Most epidemiologic studies of the association between childhood brain tumors and parental occupational exposures used a case–control study design, where the retrospective exposure assessment poses a challenge. In the majority of previous studies, the ELF-MF levels were inferred from occupations or job groups (e.g., electrical occupations) or from job exposure matrices (JEMs) based on magnetic fields measurement data. However, reliance on job titles or job groups alone may not be the most accurate method for estimating ELF-MF exposure; the use of electrical equipment in the course of work and the presence of such equipment in the work environment could be equally or more important [10]. Maternal exposure during pregnancy should receive more attention than it has so far. Although a few studies have investigated maternal occupational ELF-MF exposure, the number of mothers in the studies reporting an occupation before and during pregnancy has generally been too small to allow meaningful analyses.

The goal of this study is to evaluate whether mothers' occupational exposure to ELF-MF, immediately before and during pregnancy, is associated with an increased risk of childhood brain tumors, using individual exposure estimations or a JEM based on ELF-MF sources, work environments, and duration of exposure.

Materials and methods

Two Canadian studies were pooled; case and control selection, as well as data collection and exposure assessment methods are described separately for each study.

Case selection

Québec study

Details of this study have been described elsewhere [11]. This study was restricted to tumors occurring within the brain as defined in the International Classification of Disease for Oncology, Second Edition, using site codes C71.0–C71.9, plus cerebral meninges (C70.0), meninges undefined (C70.9), optic nerve (C72.3), pituitary gland (75.1), craniopharyngeal duct (75.2), and pineal gland (75.3). Brain tumors were classified according to the 1996 International Classification of Childhood Cancers second edition (ICCC-2) [12] as: astroglial tumors (includes optic nerve gliomas), primitive neuroectodermal tumors (PNET, consists mostly of medulloblastoma), other gliomas (includes oligodendroglioma), ependymomas (includes chorid plexus papilloma), other specified intracranial (includes craniopharyngioma, pineoblastoma/cytoma, and ganglioglioma), and other unspecified intracranial tumors (includes intracranial germ cell tumors). Primary, malignant brain tumor cases were recruited from tertiary care centers designated by governmental policy to hospitalize and treat children with cancer in the province. Tumor specimens were reviewed by pediatric neuro-pathologists. Due to budgetary constraints between 1980 and 1993 a random sample of one-third of all brain tumor cases diagnosed before 10 years of age was selected ($n = 130$). Between 1995 and 1999, all first primary, malignant brain tumor cases diagnosed in Québec before 15 years of age were invited to participate ($n = 142$). As cancer care is covered under a universal health plan for all Canadian residents, we believe a negligible number of children, if any, were treated outside the province. Study patients had to be Canadian residents at the time of diagnosis. The response rates for cases from 1980–1993 to 1995–1999 were 94.0% and 82.7%, respectively. Differences in response rates between the study periods are likely due to slightly different methods in recruiting subjects, in the earlier study period cases were recruited by the research team, while in the more recent study period cases were first approached by hospital personnel to determine interest in the study.

Ontario study

In Ontario, cases were children under the age of 15 years who were first diagnosed between October 1997 and December 2002 at five pediatric oncology centers throughout the province (Toronto (HSC), Hamilton, London, Ottawa, and Kingston), and who resided in the province at the time of diagnosis. Tumor specimens and pathology reports were reviewed by a reference pediatric neuro-pathologist. They were classified according to the WHO criteria with assigned histology codes, which are convertible to the morphology codes for the histological types using the third edition of the ICCC [13]. The resulting classification is as follows: astroglial tumors (8000, 9380–9382, 9400, 9401, 9411, 9420, 9440, and 9441), PNET (9470–9473), ependymomas (9390–9392 and 9394), other gliomas (9450), and other intracranial neoplasms (9350, 9360–9362, 9364, 9503, and 9505). ICCC-3 provides continuity with ICCC-2. During that period, 325 eligible cases were identified, among whom, 40 refused to participate, and nine could not be traced; thus, 276 interviews (85%) were completed.

Control selection

Québec study

Population-based controls (1:1 ratio) were matched to the cases on sex and age at diagnosis in the calendar year of diagnosis (i.e., a case aged four in 1995 was matched to a child of the same age free of disease in 1995). Between 1980 and 1993, controls were chosen from continuously updated family allowance files, which contain information on all children living legally in Canada. From 1995 to 1999, controls were chosen from the continuously updated provincial health insurance agency files, where current information on all families living in Québec is maintained to provide universal medical care coverage. These sources of data were the most complete census of children available during the study periods. Ten controls per case were randomly chosen from the lists according to the expected distribution of cases. The response rates for controls from 1980–1993 to 1995–1999 were 83.8% and 90.4%, respectively. Address information provided for control subjects was more accurate in the latter phase of the study.

Ontario study

In Ontario, population-based controls, frequency matched to the cases by age categories (0–1, 2–4, 5–9, and 10–14 years) at diagnosis and region of the province (using postal code areas), were randomly chosen from the Property Assessment Files of the Ontario Ministry of Finance. These files include information on all residents living legally in the province and were the only data for Ontario that enabled age-stratified sampling. In total, 722 families with an eligible child were identified, 30% refused to participate, and 488 (67%) completed the telephone interview.

Data collection

Both studies were approved by the ethics committee of each of the institutions involved and the respective provincial agencies overseeing access to information regulations. Informed consent was obtained for all study participants.

Québec study

Soon after sending a letter introducing the general purpose of the study, trained interviewers contacted the parents to schedule an appointment for an interview, which was eventually administered by telephone using structured questionnaires. One such questionnaire addressed general risk factors and potential confounding factors; another structured questionnaire was used to collect a detailed job history from the age of 18 years and on, until the end of pregnancy. It included the job title and dates on this job, the type of industry, and its name and address. For each job held by the mother from two years before pregnancy and up to birth of the index child, a semi-structured questionnaire was also used to probe for more detailed information related to the company's activities, the raw materials and final product, presence of any electrical equipment or ionizing and nonionizing radiation sources, personal protective equipment, and a detailed open-ended description of the woman's typical activities at work. Finally, for frequent job titles and/or jobs with a significant potential for occupational exposures (e.g., nurse, sewing machine operator, hairdresser, waitress, cook, textile dry cleaner, knitting, and weaving operator), a job-specific questionnaire was administered that probed more deeply into the specific tasks, the time spent at them, specific exposures related to these tasks, and the environment in which they were conducted.

Ontario study

A structured questionnaire was administered on the phone by a trained interviewer to gather information on a number of suspected risk factors including occupational history for all full and part-time (on average, a minimum of 20 h of work per week) jobs outside the home that each parent had held for at least six months; the collected information included job title and dates on this job, the main task performed, the type of industry and its name and address.

Exposure assessment

Québec study

The so-called "expert method" for assessing exposure has been described in detail elsewhere [14] and is based on the assessment of individually reported exposure data by expert chemists or hygienists. The Québec study had collected detailed parental occupational exposure information, but experts were not available to code all the ELF-MF exposure due to budget limitations. However, an estimation method and exposure matrices of maternal occupational exposure to ELF-MF by sources and work environments or job titles had been developed by the Québec research group [9], for a study of childhood acute lymphoblastic leukemia (ALL) carried out in the same province at approximately the same time. These matrices were constructed by an expert using values associated with electrical equipment and work environment, as published in the literature or based on available actual measurements. These matrices included ELF-MF estimates for 111 sources, 59 work environments, and 61 job titles. Based on this method, a pilot study was conducted to compare estimates of occupational ELF-MF exposure obtained by an educated nonexpert and an expert, using 75 case and 75 control mothers coming from Québec childhood brain tumors data. Results showed that a trained nonexpert using the published matrices from the ALL study could produce almost similar estimates of maternal occupational exposure to ELF-MF as those of an expert. In particular, for 95% of the estimates, an estimate by the nonexpert would be between 0.2 μT lower and 0.2 μT greater, than an estimate by the expert. Therefore, in the Québec study, for each job held by a mother during the two years before pregnancy up to birth, one educated nonexpert observer was trained by the expert to recognize and classify the ELF-MF sources, the potential for exposure in the work environment, and the duration of exposure. That observer assigned a weekly time-weighted average (TWA) exposure based on the published values in the matrices [9]. A TWA was calculated as the product of the magnetic field intensity of each identified source by the duration of exposure for this source; any remaining work time was multiplied by the background field level assigned to the specific work environment. The sum of products across all exposed sources and duration as well as environment and duration were divided by the total weekly hours spent at work. However, there was no useful information in the published matrix for about 18% jobs in the childhood brain tumors study; for these cases, the educated observer consulted the expert and a decision was made to assign a TWA by extrapolating exposure level from other sources in the matrix having similar electrical operations.

Each job was coded according to the seven-digit Canadian Classification and Dictionary of Occupations (CCDO) 1971 [15] and industry was coded according to the three-digit Standard Industrial Classification (SIC) 1980 [16].

Ontario study

Although essential occupational information (job tile and task as well as duration) was available from the Ontario study, it was substantially less detailed than in the Québec study. Therefore, we developed a job-exposure matrix for ELF-MF (available on request) for the Ontario study, derived from exposure information in the Québec childhood brain tumor database. In the Ontario data, there was often not enough information provided in the questionnaire to code at the same detailed level as in the Québec study; therefore, all jobs involving similar duties and similar work as those held by the mothers in the Québec study were grouped together using the first four-digits of the CCDO code. A similar grouping was done for the industries according to the first two-digits of the SIC code. The four-digit occupation codes formed a list of 121 occupation groups, and the two-digit industry codes formed a list of 47 industry groups. An exposure information table was generated from the Québec data, which included a list of four-digit occupation and two-digit industry combinations and the estimated time-weighted average exposure for each combination. These occupation and industry code combinations resulted in a total of 181 cells compiled into the JEM; each cell contained information on total number of workers for each job code, the mean value of ELF-MF, as well as the minimum and maximum value. For example, based on the individual exposure estimations of Québec childhood brain tumor data, the range of TWA for five mothers who worked as secretaries (coded 4111) in the health and social service industry (coded 86) was 0.21–0.32 μT, the mean TWA value for this job code (411186) was 0.26 μT, and the minimum and maximum values were 0.21 and 0.32 μT, respectively.

Before linking the JEM to the work histories from the Ontario data, each job held by a mother and the industry in which it was held during the two years before pregnancy and during the pregnancy were also coded to the four-digit CCDO (1971) and the two-digit SIC (1980); coding was blind to the case–control status. A mean TWA value was assigned to each combination of occupation and industry code. However, there were approximately 25% jobs which could not be linked to a cell in the JEM. For these jobs, if the occupation code was the same but the industry code was different as that in an existing JEM cell, a mean exposure value from the same occupation title but in a different industry was assigned; if, on the other hand, the occupation code could not be found in the JEM, we extrapolated the mean exposure value from the closest job type within the matrix using the questionnaire data describing the job task to confirm the assigned category.

Statistical analysis

In the Québec study individual matching was done on age and sex, whereas in the Ontario study frequency matching was based on geographic region and age groups. Because the studies used different matching strategies, unconditional logistic regression models were used with the pooled data to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs). Models were adjusted for the variables: study center, sex, and age at diagnosis of the child (in years: 0–1, 2–4, 5–9, and 10–14). Two other potential confounders, maternal age and education level, did not materially modify the ORs associated with exposure and thus were not included in the final models. Interaction between age at diagnosis and maternal ELF-MF exposure was explored.

Five maternal job or industry categories involving ELF-MF exposure that were previously found to be associated with childhood brain tumors were created for this analysis. They were electrical workers, sewing machine operators, office machine operators, food and beverage preparers, and broadcasting and entertainment industries [5, 17, 18]. An additional 35 industrial and 44 occupational categories were examined in a secondary analysis. Because many of the sub-categories were based on small numbers, ORs were reported only for categories with at least five exposed cases.

Analyses were conducted on three ELF-MF exposure metrics, as was previously done in our childhood leukemia study [19]: cumulative exposure, average exposure, and peak exposure. Cumulative exposure [expressed as exposure microTesla-days, (μT-days)] was calculated as the sum across all jobs of the product of the TWA for each job held times its duration. For example, if a mother held a job during two years before pregnancy with an intensity value of 0.2 μT and worked 150 days, changed her job to another job code with an intensity level of 0.16 μT, and worked 100 days, that mother's cumulative exposure for magnetic fields is $(0.2 \times 150 + 0.16 \times 100) = 46$ μT-days. Average exposure (i.e., cumulative exposure divided by the duration of exposure) in this case is (46 μT-days/250) = 0.18 μT. Cumulative and average exposures were classified into two categories, at or above the 90th percentile of the distribution, and below the 90th percentile, among all study women (working and nonworking). This cut-point was selected based on previous studies; first, a meta-analysis of residential exposures in which a moderately increased risk of childhood brain tumors was observed only among children exposed at high level (residential magnetic fields exposure above 0.3 or 0.4 μT) [3]; and second, the fact that 0.4 μT is a level above which residential magnetic fields were associated with childhood leukemia [7]. The peak exposure for an occupation was measured as weekly TWA and dichotomized at 0.4 μT, for this same reason.

Using these three exposure metrics, analyses were conducted in two time windows, i.e., the first was for the two-year period before pregnancy, reflecting the continuity of jobs over this period of time, and the second was for the pregnancy period. For tumor-specific analyses, cases were classified into three major histological types which are astroglial tumors, PNET, and other gliomas, including ependymomas, oligodendrogliomas, and other unspecified gliomas.

Results

The distribution of tumor types (Table 1) was quite similar between the two studies. The distribution of all characteristics was similar between cases and controls in the Québec study. In the Ontario study, this was also the case except for the age and sex distributions of study subjects. The level of education was lower in the Québec study, reflecting in part the fact that recruitment in this study dates back further than in the Ontario study. In the pooled data, child's age differed markedly between cases and controls carrying the impact of these distributions being different between the cases and controls in the Ontario study.

Of the five maternal job or industry categories where an association with childhood brain tumors was previously suggested (see above), we found a elevated risk among children of mothers employed as sewing machine operators for all brain tumors combined (OR = 2.3, 95% CI = 1.0–5.4), as well as for astroglial tumors (OR = 2.3, 95% CI = 0.8–6.3) and other gliomas (OR = 2.9, 95% CI = 0.8–11.7) (Table 2). An elevated risk for other gliomas was also found for mothers working as food and beverage preparers (OR = 2.9, 95% CI = 1.4–6.3). There was no increased risk associated with the categories secretaries and typists or broadcasting and entertainment industries. Although risk of childhood brain tumors in the offspring of electrical workers has also been suggested to be increased, there was only one exposed case and results were not reported in the table.

Where at least five cases were exposed, analyses of other occupation and industry groups were carried out. A statistically significant association was observed for other gliomas in the food and beverage service group (OR = 2.6, 95% CI = 1.2–5.5). Elevated risk for other gliomas was also found for mothers working as nurses (OR = 2.1, 95% CI = 1.0–5.0) or for all tumors combined in the health services group (OR = 1.3, 95% CI = 1.0–1.8). No other associations between childhood brain tumors and maternal occupations or industries before birth were observed.

Median ELF-MF levels were similar for cases and control groups in each study when using cumulative and average metrics among all women and working women (Table 3). Compared to Québec study, the Ontario median levels for the cumulative metric were slightly lower before conception and slightly higher during pregnancy; the median levels for the average metric were similar in both studies.

For the two-year period before pregnancy, the absolute number of women considered exposed for any of the three ELF-MF exposure metrics was somewhat higher in the Québec than in the Ontario study, despite a similar number of cases and a smaller number of controls (Table 4). The ORs in the Quebec study were slightly lower than those observed in the Ontario study for cumulative and average exposure metrics. We did not find any association with maternal occupational ELF-MF exposure in either study. During the entire pregnancy period, the ORs were similar as those observed for the period before conception for each

Table 1 Socio-demographic characteristics of cases with childhood brain cancer and controls by study center

	Québec		Ontario		Pooled	
	Cases ($n = 272$)	Controls ($n = 272$)	Cases ($n = 276$)	Controls ($n = 488$)	Cases ($n = 548$)	Controls ($n = 760$)
Child age (years)[a]						
<2	22 (8.1)	21 (7.7)	42 (15.2)	17 (3.5)	64 (11.7)	38 (5.0)
2–4	99 (36.4)	100 (36.8)	57 (20.7)	65 (13.3)	156 (28.5)	165 (21.7)
5–9	121 (44.5)	121 (44.5)	93 (33.7)	188 (38.5)	214 (39.1)	309 (40.7)
≥10	30 (11.0)	30 (11.0)	84 (30.4)	218 (44.7)	114 (20.8)	248 (32.6)
Child's sex						
Male	160 (58.8)	160 (58.8)	155 (56.2)	247 (50.6)	315 (57.5)	407 (53.6)
Female	112 (41.2)	112 (41.2)	121 (43.8)	241 (49.4)	233 (42.5)	353 (46.4)
Maternal age at child's birth (years)[b]						
<35	253 (93.4)	257 (94.5)	241 (87.3)	414 (84.8)	494 (90.3)	671 (88.3)
≥35	18 (6.6)	15 (5.5)	35 (12.7)	74 (15.2)	53 (9.7)	89 (11.7)
Race[c]						
White	254 (93.4)	263 (96.7)	241 (88.6)	448 (92.0)	495 (91.0)	711 (93.7)
Nonwhite	18 (6.6)	9 (3.3)	31 (11.4)	39 (8.0)	49 (9.0)	48 (6.3)
Mother's level of education[d]						
None or primary school	12 (4.4)	6 (2.2)	3 (1.1)	1 (0.2)	15 (2.8)	7 (0.9)
Secondary school	133 (48.9)	148 (54.6)	68 (24.9)	118 (24.2)	201 (36.7)	266 (35.1)
College or university	127 (46.7)	117 (43.2)	202 (74.0)	369 (75.6)	329 (60.5)	486 (64.0)
Employment						
Two years before pregnancy						
No	57 (21.4)	59 (22.1)	55 (20.9)	99 (20.4)	112 (21.1)	158 (21.0)
Yes	210 (78.6)	208 (77.9)	208 (79.1)	386 (79.6)	418 (78.9)	594 (79.0)
During pregnancy						
No	96 (36)	90 (33.7)	73 (27.8)	133 (27.4)	169 (31.9)	223 (29.6)
Yes	171 (64.0)	177 (66.3)	190 (72.2)	352 (72.6)	361 (68.1)	529 (70.4)
Type of tumor						
Astroglial tumors	120 (44.1)		119 (43.1)		239 (43.6)	
PNET	80 (29.4)		65 (23.6)		145 (26.5)	
Other gliomas[e]	42 (15.4)		39 (14.1)		81 (14.8)	
Other tumors	30 (11.0)		53 (19.2)		83 (15.1)	

PNET primitive neuroectodermal tumors

[a] Age at diagnosis for cases and interview for controls

[b] Mother's date of birth missing for one case in Québec study

[c] Race missing for four cases and one controls in Ontario study

[d] Mother's education missing for one control in Québec study and three cases in Ontario study

[e] Other gliomas include ependymomas, oligodendrogliomas, and other unspecified gliomas

exposure metric. However, when considering histological subgroups for both studies together (Table 5), an elevated risk for astroglial tumors was associated with the average exposure metric (OR = 1.5, 95% CI = 1.0–2.4) before conception. During the entire pregnancy period, a significantly elevated risk was also observed for the average metric with astroglial tumors and all tumors combined (OR = 1.6, 95% CI = 1.1–2.5 and OR = 1.5, 95% CI = 1.1–2.2, respectively).

No significant interactions between maternal ELF-MF exposure and age at diagnosis of the child were found in the analysis.

Discussion

In this study, we did not find strong associations between childhood brain tumors and mothers being potentially

Table 2 Adjusted Odds ratios (OR)[a] of childhood brain tumors for selected maternal occupational and industries during the three-year period before birth according to main histological subgroups

Occupations/industries	Controls ($n = 760$)	All tumors ($n = 548$)		Astroglial tumors ($n = 239$)		PNET ($n = 145$)		Other gliomas[b] ($n = 81$)	
	No	No	OR (95% CI)	No	OR (95% CI)	No	OR (95% CI)	No	OR (95% CI)
Occupations									
Secretaries and typists	72	54	1.1 (0.7–1.6)	25	1.1 (0.7–1.9)	13	1.0 (0.5–1.8)	8	1.1 (0.5–2.4)
Sewing machine operators	8	16	2.3 (1.0–5.4)	7	2.3 (0.8–6.3)	3	1.5 (0.4–5.8)	3	2.9 (0.8–11.7)
Food and beverage preparers	35	32	1.3 (0.8–2.2)	9	0.8 (0.4–1.6)	10	1.5 (0.7–3.2)	10	2.9 (1.4–6.3)
Food and beverage processors	8	8	1.4 (0.5–3.9)	3	1.2 (0.3–4.6)	3	2.2 (0.5–8.6)	1	1.2 (0.1–9.8)
Textile, fur, and leather fabricators	19	19	1.1 (0.6–2.2)	8	1.0 (0.4–2.4)	5	1.1 (0.4–3.0)	3	1.1 (0.3–3.8)
Material packagers	6	11	2.2 (0.8–6.2)	6	2.8 (0.9–9.2)	3	1.8 (0.4–7.8)	1	1.5 (0.2–12.8)
Nurse and assistant	37	25	1.1 (0.6–1.7)	11	1.1 (0.5–2.2)	6	0.9 (0.4–2.2)	7	2.1 (1.0–5.0)
Clerk	240	166	1.0 (0.8–1.3)	82	1.2 (0.9–1.6)	34	0.7 (0.4–1.0)	23	0.9 (0.5–1.4)
Sale workers	36	29	1.1 (0.7–1.9)	11	0.9 (0.5–1.8)	8	1.3 (0.6–2.8)	3	0.7 (0.2–2.2)
Teachers and professors	45	33	1.1 (0.7–1.7)	14	1.1 (0.5–2.0)	11	1.3 (0.6–2.6)	5	1.2 (0.5–3.2)
Lawyer and related	7	6	1.5 (0.5–4.6)	2	1.1 (0.2–5.5)	2	1.8 (0.4–9.3)	1	1.9 (0.3–15.6)
Managers and administrators	76	40	0.8 (0.5–1.2)	16	0.8 (0.5–5.5)	12	1.0 (0.5–2.0)	9	1.4 (0.6–3.0)
Industries									
Broadcasting and entertainment	32	18	1.0 (0.5–1.7)	10	1.2 (0.6–2.4)	4	0.7 (0.2–2.2)	1	0.3 (0.1–2.5)
Food and beverage industries	10	12	1.6 (0.7–3.8)	5	1.5 (0.5–4.6)	4	2.4 (0.7–8.3)	1	0.9 (0.1–7.4)
Textile and clothing	15	22	1.6 (0.8–3.1)	10	1.5 (0.7–3.5)	6	1.5 (0.5–4.0)	3	1.3 (0.3–4.6)
Wholesale and retail	63	54	1.3 (0.9–1.9)	26	1.4 (0.9–2.4)	13	1.2 (0.6–2.2)	11	1.7 (0.4–3.4)
Finance and insurance	51	31	0.9 (0.6–1.5)	19	1.4 (1.8–2.4)	5	0.5 (0.2–1.3)	6	1.1 (0.5–2.8)
Health service	107	89	1.3 (1.0–1.8)	39	1.3 (0.9–2.0)	23	1.3 (0.8–2.2)	15	1.5 (0.8–2.7)
Office unspecified	11	12	1.2 (0.5–2.8)	7	1.6 (0.6–4.2)	4	1.3 (0.4–4.1)	1	0.7 (0.1–5.4)
Food and beverage service	36	37	1.4 (0.8–2.2)	11	0.9 (0.4–1.8)	10	1.3 (0.6–2.8)	10	2.6 (1.2–5.5)
Business service	93	67	0.9 (0.6–2.2)	28	0.8 (0.5–1.3)	17	0.8 (0.4–1.4)	12	1.1 (0.6–2.1)
Educational service	62	37	0.9 (0.6–1.4)	18	1.0 (0.6–1.8)	10	1.0 (0.5–2.1)	4	1.5 (0.5–4.7)
Transportation	9	6	1.0 (0.4–2.9)	5	2.0 (0.7–6.2)	0	–	0	–
Government service	29	17	1.0 (0.5–2.8)	6	0.8 (0.3–2.0)	3	0.6 (0.2–2.2)	3	1.2 (0.4–4.2)

PNET primitive neuroectodermal tumors

[a] ORs were calculated adjusted for child's age, sex, and study center

[b] Other gliomas include ependymomas, oligodendrogliomas, and other unspecified gliomas

exposed to ELF-MF before and during pregnancy through their occupations or the industries in which they worked. Except for sewing machine operators, most categories of occupations or industries with a higher ELF-MF exposure had only one subject. However, children of sewing machine operators had an OR indicative of a twofold increase in the risk of all tumors combined as well as for astroglial tumors and other gliomas. A similar observation was also reported in our childhood leukemia study [19]. We used three exposure metrics (cumulative, average, and maximum level) to further analyze quantitative occupational ELF-MF exposure. There was some evidence that an elevated risk was observed for astroglial tumors with average exposure metric before conception. During the entire pregnancy period, a significantly elevated risk was also observed for astroglial tumors and all tumors combined with the average metric.

Only one previous epidemiologic study has examined the risk of childhood brain tumors related to maternal quantitative occupational magnetic fields exposure. Feychting et al. [6] conducted a cohort study in Sweden to examine the association between parental exposure to magnetic fields and the risk of cancers in their offspring. Information about parental occupations was linked to a JEM developed for a male population. In that study, no association between childhood brain tumors and maternal occupational mean magnetic fields exposure before conception was observed. However, the study was limited by the fact that the JEM developed for male workers may not have been completely applicable to women, and about 40%

Table 3 Median levels of maternal occupational exposure to extremely low frequency magnetic fields for each center

	Québec		Ontario		Pooled	
	All women	Only working women	All women	Only working women	All women	Only working women
Before conception						
Cumulative exposure (μT-days) [Median (min, max)]						
Cases	106.5 (0, 1095.0)	145.1 (2.4, 1095.0)	102.2 (0, 1237.7)	138.7 (0.2, 1237.7)	102.2 (0, 1237.7)	141.9 (0.2, 1237.7)
Controls	102.2 (0, 1286.6)	146.0 (2.2, 1286.6)	100.0 (0, 1237.7)	131.4 (4.8, 1237.7)	102.2 (0, 1286.6)	139.0 (2.2, 1286.6)
Average exposure (μT) [Median (min, max)]						
Cases	0.2 (0, 3.0)	0.2 (0, 3.0)	0.2 (0, 1.7)	0.2 (0, 1.7)	0.2 (0, 3.0)	0.2 (0, 3.0)
Controls	0.2 (0, 1.8)	0.2 (0, 1.8)	0.2 (0, 1.7)	0.2 (0, 1.7)	0.2 (0, 1.8)	0.2 (0, 1.8)
During pregnancy						
Cumulative exposure (μT-days) [Median (min, max)]						
Cases	21.3 (0, 247.9)	49 (0.2, 247.9)	36.2 (0, 457.8)	54.3 (1.1, 457.8)	27.3 (0, 457.8)	50.3 (0.2, 457.8)
Controls	24.2 (0, 266.4)	50.8 (0.3, 266.4)	34.2 (0, 457.8)	60.1 (0.5, 457.8)	29.3 (0, 457.8)	50.2 (0.3, 457.8)
Average exposure (μT) [Median (min, max)]						
Cases	0.1 (0, 0.9)	0.2 (0, 0.9)	0.1 (0, 1.7)	0.2 (0, 1.7)	0.1 (0, 1.7)	0.2 (0, 1.7)
Controls	0.1 (0, 1.8)	0.2 (0, 1.8)	0.1 (0.1, 1.7)	0.2 (0, 1.7)	0.1 (0, 1.8)	0.2 (0, 1.8)

Table 4 Adjusted Odds ratios (ORs) for childhood brain tumor associated with maternal occupational exposure to extremely low frequency magnetic fields for each study center and for both centers together

	Québec			Ontario			Pooled
	Cases	Controls	OR (95% CI)[a]	Cases	Controls	OR (95% CI)[a]	OR (95% CI)[b]
Two-year period before pregnancy							
Cumulative exposure ≥90th percentile (≥214.8 μT-days)	40	37	1.1 (0.7–1.8)	24	29	1.5 (0.9–2.9)	1.3 (0.9–2.0)
Average exposure ≥90th percentile (≥0.30 μT)	46	40	1.2 (0.7–1.9)	23	28	1.5 (0.8–2.7)	1.4 (1.0–2.1)
Maximum exposure (≥0.4 μT)	19	14	1.4 (0.7–2.8)	11	23	0.8 (0.4–1.8)	1.1 (0.7–1.8)
During pregnancy							
Cumulative exposure ≥90th percentile (≥73.6 μT-days)	31	30	1.1 (0.6–1.8)	32	36	1.7 (0.9–2.8)	1.4 (0.9–2.0)
Average exposure ≥90th percentile (≥0.28 μT)	43	38	1.3 (0.7–1.9)	34	36	1.8 (1.0–2.9)	1.5 (1.1–2.2)
Maximum exposure (≥0.4 μT)	14	12	1.2 (0.5–2.6)	12	18	1.2 (0.5–2.5)	1.2 (0.7–2.1)

[a] ORs were calculated adjusted for child's age and sex

[b] ORs were calculated adjusted for child's age, sex, and study center

of the mothers could not be included in the analyses because no measurements were available for them. Furthermore, studying total brain tumors as a single entity may mask or attenuate a causal association.

Since potential biological mechanisms through which ELF-MF may cause carcinogenic effects have not yet been identified, the relevant exposure metrics for the effect of ELF-MF are speculative. Whereas we used three metrics, others may be relevant also to capture transient or intermittent exposure; the latter may have a greater potential to cause genotoxic effects [20, 21] than the exposure estimated by our three metrics. In this study, the risk estimates for all the three metrics were fairly consistent in both exposure periods.

All other previous epidemiologic studies have evaluated an association between childhood brain tumors risk and maternal occupational exposure using job titles or groups. One such study was conducted in the UK [5]; women were first classified based on occupations which possibly involved electric and magnetic fields (EMF) exposure. Mother's occupation as sewing machinist during the preconception period and during pregnancy was not a risk factor for all brain tumors combined. However, the relative risk for mothers who held work in the textile industry (other than sewing

Table 5 Adjusted Odds ratios (ORs)[b] for childhood brain tumors for maternal occupational exposure to extremely low frequency magnetic fields according to main histological subgroups

	Controls (n = 760)	Astroglial tumors (n = 239)		PNET (n = 145)		Other gliomas[b] (n = 81)	
	No	No	OR (95% CI)	No	OR (95% CI)	No	OR (95% CI)
Two-year period before pregnancy							
Cumulative exposure ≥90th percentile (≥214.8 μT-days)	66	28	1.3 (0.8–2.1)	17	1.2 (0.7–2.2)	11	1.6 (0.8–3.2)
Average exposure ≥90th percentile (≥0.30 μT)	68	34	1.5 (1.0–2.4)	14	0.9 (0.5–1.6)	11	1.5 (0.8–2.9)
Maximum exposure (≥0.4 μT)	37	14	1.3 (0.6–2.3)	7	1.0 (0.4–2.3)	3	0.8 (0.2–2.7)
During pregnancy							
Cumulative exposure ≥90th percentile (≥73.6 μT-days)	66	29	1.4 (0.9–2.3)	15	1.2 (0.6–2.2)	11	1.7 (0.8–3.3)
Average exposure ≥90th percentile (≥0.28 μT)	74	38	1.6 (1.1–2.5)	17	1.1 (0.6–2.0)	12	1.6 (0.8–3.1)
Maximum exposure (≥0.4 μT)	30	15	1.6 (0.8–3.1)	5	0.9 (0.3–2.3)	1	0.3 (0.1–2.4)

PNET primitive neuroectodermal tumors

[a] ORs were calculated adjusted for child's age and sex and study center

[b] Other gliomas include ependymomas, oligodendrogliomas, and other unspecified gliomas

machinist) before conception with likely EMF exposure was significantly elevated (RR = 1.44, 95% CI = 1.03–2.01). These results are compatible with our findings for sewing machine operators and all brain tumors combined.

McKean-Cowdin et al. [17] found an all tumor OR of 2.4 (95% CI = 1.0–5.6) for mothers employed in the broadcasting and entertainment industries (motion picture, radio, television, or theatre) during the preconception period, and an OR of 1.5 (95% CI = 1.0–2.1) for those whose tasks included office machine operation (stenography and typing), as well as an OR of 1.6 (95% CI = 1.1–2.5) for astroglial tumors among those working as food preparers. For the categories secretaries and typists and broadcasting and entertainment industries, no significantly increased risks were observed in our study; however, we observed a similar result among those working as food and beverage preparers for other gliomas.

Kuijiten et al. [22] observed an increased risk of astroglial tumors for mothers working as nurses [OR of 2.2 (95% CI = 0.7–8.1)], and the risk was higher for children diagnosed before age four. On the other hand, Olsen et al. [23] also reported an OR of 1.4 ($p < 0.05$) for all tumors combined among children of women working as nurses. We also found an increased risk for other gliomas and all tumors combined for mothers working as nurses and in the health service industries, respectively. Working as a nurse or in health services also involves potential exposure to chemicals or solvents, which may themselves be risk factors for childhood brain tumors [24, 25].

In most epidemiologic studies of the association between childhood brain tumors and parental occupational exposures, the retrospective exposure assessment poses a significant challenge and misclassification of exposure is a common concern. In this study, we used two exposure assessment methods, i.e., individual exposure estimations and a job exposure matrix. The potential misclassification biases are discussed for each method.

To our knowledge, this study is the first to use individual exposure estimations (Québec study) based on the main determinants of exposure such as sources, work environments, as well as duration, to examine associations between maternal ELF-MF exposure and childhood brain tumors. Nevertheless, some misclassification has likely occurred, and possibly more so when the information collected from mothers was not detailed enough to accurately estimate the exposure duration. In addition, reliance on published ELF-MF levels associated with source and work environment, as found in the matrices we used, may have limitations since some sources or environments may have many published values, while others may have few or none. Furthermore, the published measurements may have been taken at a different time from that when the actual exposure occurred, and magnetic fields exposure within occupations may well have changed over time due to increased use of electrical equipments or improved manufacturing processes. However, this exposure assessment was not adjusted for possible effects due to the era in which the job was held because there is little or no specific information available on the change of magnetic fields with time for the various sources or environments. For sources or environments where there were no published values, estimated levels were assigned by an expert based on reviewing of the measurement campaigns conducted in the province of Québec. This method of assigning values to estimate magnetic fields exposure has also been employed in other studies [19, 26].

We believe that the JEM for ELF-MF, derived from individual exposure information from the Québec data was probably the more feasible approach to estimate Ontario's occupational exposures due to the minimal available information. However, since some jobs involve many different tasks with widely varying levels of exposure, based on the individual assessment, an average exposure level was used for these job titles. This could have resulted in greater nondifferential misclassification of exposure than for individual estimation [27]. Furthermore, the fact that we used the Québec ELF-MF values for job titles with very few subjects, to assign them to the Ontario data, may have resulted in unstable exposure estimates. Nevertheless, a JEM based on sources, work environments, and duration, in contrast with JEMs based solely on source measurements without considering work environments, is expected to improve the precision of exposure estimates [10]. Although the reliability of the JEM constructed from the Québec population but applied to the Ontario population was not fully evaluated, Québec and Ontario are neighboring provinces in central Canada, have similar economies and are quite similar with respect to types of industrial practice. There were approximately 25% of jobs in the Ontario data for which occupation and industry information was not sufficient to find a correspondence in the Québec data. For these cases, we extrapolated the mean exposure value from the closest job type within the matrix using the job task description to confirm the assigned category. This could be an additional source of nondifferential misclassification in our data.

We were unable to assess the effect of home exposure to ELF-MF since this variable was not measured; however, the proportion of nonworking women, and the distribution of mother's age and education level were quite similar between cases and controls in each study, reducing the potential for marked differential home exposures between the mothers of cases and controls.

In conclusion, results are suggestive of a possible association between maternal occupational ELF-MF exposure and certain brain tumors in their offspring. Future studies should confirm this association with improved exposure assessment. Different and specific exposure scenarios may have a different potential to cause carcinogenic effects. Although no such clue was provided in our data from the use of three exposure metrics, other aspects of exposure, in particular, transient or intermittent exposure, should also be taken into account in future studies.

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