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Original Article

Occupational Exposure to Electromagnetic Fields by Questionnaire in Relation to Risks of Brain Cancer: Cell-type Specificity

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Purpose: The aim of this study was to address the associations between occupational exposure to electromagnetic fields (EMF) and the risk of brain tumors across different histological types.
Materials and Methods: A total of 111 cases of primary brain tumors and 235 controls were collected for a hospital-based case-control study. The exposure assessment separated workers into three different groups (non-exposure, possible-exposure, and explicit-exposure) of occupational exposure depending on different strengths of EMF.
Results: A significantly increased risk of brain tumors was observed among men held jobs with "explicit-exposure" to EMF relative to those with "non-exposure" (OR = 7.37, 95% CI: 1.36-40.03). The OR for acoustic neuroma cases was 7.39 (95% CI: 1.91-28.54) with "explicit- exposure" to EMF relative to those with "non-exposure", and the OR for glioma cases was 6.22 (95% CI: 1.51-25.73) in the "possible-exposure" group relative to the "non-exposure" group.
Conclusion: Our findings of questionnaire support the association of occupational exposure to EMF in the development of both glioma and acoustic neuroma.

Key words: brain cancer, electromagnetic fields, occupational exposure, case-control study

Introduction

Brain tumors are rare but often fatal. In 2006, it was estimated that there were nearly 667 new cases diagnosed and 401 new deaths from primary brain tumors in Taiwanese adults[1]. The etiology of brain tumors is not well understood. Decades of studies have been conducted in an effort to identify the cause of brain tumors. Ionizing radiation[2, 3], organic solvents (e.g., vinyl chlorides[4-6], pesticides[7]), genetic predisposition[8], and electromagnetic fields (EMF) have been implicated

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as the risk factors for brain tumors[9]. As a result of the quick development of electrosurgical devices during the twentieth century, the opportunity for occupational exposure to EMF is increasing. Previous studies suggesting the association between occupational exposure to EMF and brain tumors have generally provided weak or no evidence of a causal relationship. The first report of an association between occupational exposure to EMF and brain tumors was published in 1985[10], which was later corroborated in other studies[11-15]. Many epidemiological studies have found a positive relationship between exposure to EMF and the risk of brain tumors[11, 12], while others have not[13, 14]. Furthermore, data from previous studies on pathological cell types of brain tumors are quite limited. A report on male subjects in a population-based case-control study conducted in Central Sweden showed a tendency toward an increased risk for glioma among men occupationally exposed to EMF with mean values of more than 0.4 μT[15]. Using job exposure matrices (JEMs) combined with professional judgment to evaluate quantitatively occupational exposure to EMF levels by job title, a study using data from the Canadian National Enhanced Cancer Surveillance System reported a positive association between the duration of occupational exposure to EMF, with exposure greater than 3.0 mG, and glioblastomas[16]. However, a hospital-based case-control study has shown no association between occupational exposure to EMF, assessed using JEMs, and an increase in the risk of developing glioma, glioblastoma, or meningoma[17]. Therefore, the association between occupational exposure to EMF and pathological cell types of brain tumors is not yet certain. Hence, the aim of this study was to explore whether brain tumors associated with occupational exposure to EMF have cell type specificity.

Materials and Methods

The relationship between occupational exposure to electromagnetic fields and brain cancer was investigated using a hospital-based case-control study between September 2004 and February 2005. A total of 111 brain cancer cases from the Neurosurgery Department at Chung Shan Medical University Hospital in Taiwan were enrolled in this study. Each single case was a primary brain tumor. Patients with metastatic brain tumors and angiomas were excluded from this study. The study cases were diagnosed and confirmed by medical specialists and pathologists. Controls were also selected at the same hospital and any cases with diseases possibly caused by exposure to electromagnetic fields were eliminated from the control group. The 235 controls were collected from the Department of Neurosurgery, the Department of Neurology, the Department of Orthopedics, and from other hospitalized patients. The exposure information for both case and control groups were collected by personal interviews and questionnaires including personal information, exposure history to electronic fields, history of illness, family history of cancer, smoking and drinking status. Informed consent was obtained from each subject after a full explanation of this study.

A questionnaire was used to understand the patients' working environment from the start of their employment until the diagnosis of the brain tumor. Those included in the study had to be employed for at least half a year. From this assessment, we separated workers into three different groups according to the level of occupational exposure to EMF. The three exposure groups were "non-exposure," "possible-exposure," and "explicit-exposure."[10] The occupational barcode in this questionnaire was based on 1990 job classifications.[18]

Statistical analysis of the data was performed using the SAS Software Package (Version 9.12; SAS Institute Inc, Cary, NC). The association between case and control groups categorized by variables was determined by Chi-square test or Fisher's exact test. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for brain tumors were calculated from unconditional logistic regression models according to occupational exposure to electromagnetic fields. The analysis of brain tumors was further performed by using histopathology grouping. Statistical results were considered to be significant at $p < 0.05$.

Results

Table 1 shows the basic demographic characteristics for the brain tumor cases and controls. The characteristics include: age, sex, education level, and family background. The table indicates that the subjects in the case group were older than those in the control group, with 6.31% of the case group and 12.34% of the controls under thirty years old. Also, the number of females in the case group was higher than in the control group. The education level of the case group was also higher. For example, 29.73% of the people in the case group graduated from senior high school, while in the control group, most of the people graduated from elementary school (30.64%). After biometry testing, it was discovered that there was no significant difference in age, sex, and educational level within the case and control groups. There was no significant difference in the race of the population as well.

A total of 111 cases of primary brain tumors and 235 controls were collected from a hospital-based case control study. After an assessment of exposure, we separated workers into three different groups according to the level of occupational exposure to EMF. The three exposure groups were "non-exposure", "possible exposure", and "explicit-exposure". The "explicit-exposure" group included factory engineers, mold designers, factory production line operators (of fountains and athletic accessories), factory workers who use chainsaws, and production line engineers. The "possible exposure" group included ironworkers, truck drivers, automobile technicians, tailors, remodeling

Table 1. Characteristics of cases and controls.

Characteristics	Cases (N = 111)		Control (N = 235)		χ^2	*p*-value[a]
	n	%	*n*	%		
Age group (years)					3.395	0.181
≤ 30	7	6.31	29	12.34		
31-65	75	67.57	141	60.00		
> 65	29	26.13	65	27.66		
Sex					2.875	0.101
Male	38	34.23	103	43.83		
Female	73	65.77	132	56.17		
Education level					8.984	0.107
Illiterate	21	18.92	46	19.57		
Elementary school	22	19.82	72	30.64		
Junior high school	19	17.12	40	17.02		
Senior high school	33	29.73	44	18.72		
University	14	12.61	30	12.77		
Graduate school	2	1.8	1	0.42		
Unknown	0	0.00	2	0.86		
Family background					6.286	0.396
Taiwanese	97	87.39	203	86.38		
Hakka	7	6.31	15	6.38		
Aborigines	2	1.80	0	0.00		
Mainland	4	3.60	14	5.96		
Other	0	0.00	1	0.43		
Unknown	1	0.90	2	0.85		

Data are presented as samples and percentage. The values are significantly different between case and control groups with $p < 0.05$.
[a] We used Chi-square test or Fisher's exact test for categorical data.

Table 2. Unadjusted odds ratios (ORs) and 95% confidence interval (95% CI) for the risk of occupational exposure to electromagnetic fields.

Exposure Level	Cases (*N* = 111)		Controls (*N* = 235)		OR	95%CI
	n	%	*n*	%		
Total number						
Explicit-exposure	9	8.11	7	2.98	3.04	1.09-8.49*
Possible-exposure	31	27.93	54	22.98	1.36	0.81-2.89
Non-exposure	71	63.96	168	71.49	1.00	-
Uncertain	0	0.00	6	2.55	-	-
Male	*n* = 38		*n* = 103			
Explicit-exposure	5	13.16	4	3.88	4.53	1.09-18.87*
Possible-exposure	17	44.74	37	35.92	1.67	0.75-3.70
Non-exposure	16	42.10	58	56.32	1.00	-
Uncertain	0	0.00	4	3.88	-	-
Female	*n* = 73		*n* = 132			
Explicit-exposure	4	5.48	3	2.27	2.67	0.58-12.33
Possible-exposure	14	19.18	17	12.88	1.65	0.76-3.59
Non-exposure	55	75.34	110	83.33	1.00	-
Uncertain	0	0.00	2	1.52	-	-

Results from unconditional logistic regression analysis. The results are presented as OR and 95% CI.
*$p < 0.05$.a We used Chi-square test or Fisher's exact test for categorical data.

workers, hair designers, accountants, shoemakers, graphic designers, and computer information technicians in a sugarcane factory. Others such as homemakers, farmers, nurses, students, martial arts instructors, servers, retailers, babysitters, soap manufacturers, and department store clerks were classified into the "non-exposure" group.

Table 2 summarizes univariate analysis of occupational exposure levels to EMF and brain tumors. Of the 111 brain tumor cases, 9 were classified as "explicit-exposure to EMF," 31were categorized as "possible exposure to EMF," and 71 were categorized as "non-exposure to EMF". Of the 235 control group cases, 7 were grouped as "explicit-exposure," 54 were "possible exposure," and 168 were "non-exposure." There were 6 cases where the level of EMF was uncertain. After analysis by univariate logistic regression, we used the "non-exposure to EMF" group as a reference and compared it with "possible exposure to EMF." The OR was 1.36 (95% CI: 0.81-2.89). When compared with the "explicit-exposure to EMF" group, the OR was 3.04 (95% CI: 1.09-8.49), which is significant. When we analyzed gender, we set the "non-exposure to EMF" group as a reference. The OR value was 1.67 (95% CI: 0.75-3.70) when compared with "possible exposure to EMF" and was 4.53 (95% CI: 1.09-18.87) with "explicit-exposure to EMF" for men. The OR value was 1.65 (95% CI: 0.76-3.59) and 2.67 (95% CI: 0.58-12.33) for women, respectively.

As can be seen in Table 3, when applying multiple logistic regression, after adjusting for age, gender, smoking, drinking and home environment (in or out of the vicinity of power plants), we found an OR of 1.09 (95% CI: 0.56-2.12) for "possible exposure to EMF" and was 4.68 (95% CI: 1.50-14.57) for "explicit-exposure to EMF" when compared with "non-exposure to EMF" as a reference group. The trend found in this gender analysis was similar to the results of the univariate logistic regression analysis. When comparing "explicit-exposure to EMF" with "non-exposure to EMF" as a reference group, the OR value was 7.37 (95% CI: 1.36-40.03) for men and 2.42 (95% CI: 0.51-11.56) for women. In the comparison of "possible exposure to EMF" and "non-exposure to EMF," the OR value for men was 1.69 (95% CI: 0.65-4.43) and 0.85 (95% CI: 0.29-2.41) for women.

Table 4 shows the results for pathological cell

Table 3. Adjusted odds ratios (ORs) and 95% confidence interval (95% CI) for brain tumors according to occupational exposure to electromagnetic fields.

Exposure Leve	Cases (*N* = 111)		Controls (*N* = 235)		OR[a]	95%CI
	n	%	*n*	%		
Total number						
Explicit-exposure	9	8.11	7	2.98	4.68	1.50-14.57*
Possible-exposure	31	27.93	54	22.98	1.09	0.56-2.12
Non-exposure	71	63.96	168	71.49	1.00	-
Uncertain	0	0.00	6	2.55	-	-
Male	*n* = 38		*n* = 103			
Explicit-exposure	5	13.16	4	3.88	7.37	1.36-40.03*
Possible-exposure	17	44.73	37	35.92	1.69	0.65-4.43
Non-exposure	16	42.11	58	56.32	1.00	-
Uncertain	0	0.00	4	3.88	-	-
Female	*n* = 73		*n* = 132			
Explicit-exposure	4	5.48	3	2.27	2.42	0.51-11.56
Possible-exposure	14	19.18	17	12.88	0.85	0.29-2.41
Non-exposure	55	75.34	110	83.33	1.00	-
Uncertain	0	0.00	2	1.52	-	-

Results from multiple unconditional logistic regression analysis. The results are presented as OR and 95% CI.
[a] Model also included age, gender, smoking, drinking, and home environment (such as in or out of the vicinity of power plants, and electronic towers).
*$p < 0.05$.

types of brain tumors (including meningiomas, pituitary adenomas, acoustic neuromas, gliomas and others) and estimates for those grouped as "possible-exposure" and "explicit-exposure" compared to those who have never been exposed to EMF. For gliomas with possible-exposure to EMF, the OR value was 6.22 (95% CI: 1.51-25.73) but for other pathological cell types of brain tumors the odds ratio was non-significant. The OR value for explicit-exposure to EMF was 7.39 (95% CI: 1.91-28.54) in acoustic neuromas. For this exposure category, adjustment for potential confounders made no material difference in the results.

Discussion

In this hospital-based case-control study, we found that as a whole, an increase in occupational exposure to EMF will increase the risk of

Table 4. Crude Odds Ratios (ORs) and 95% confidence interval (95% CI) for brain tumors relative to occupational exposure to electromagnetic fields in different pathology types.

Exposure level	Control (n = 229)	Meningioma Case (n = 44)	Meningioma OR (95% CI)	Pituitary adenoma Case (n = 14)	Pituitary adenoma OR (95% CI)	Acoustic neuroma Case (n = 21)	Acoustic neuroma OR (95% CI)	Gliomaa[a] Case (n = 10)	Gliomaa[a] OR (95% CI)	Others[b] Case (n = 19)	Others[b] OR (95% CI)
Explicit- exposure	7	2	1.55 (0.31-7.81)	1	2.18 (0.25-19.35)	4	7.39 (1.91-28.54)*	1	8.00 (0.74-86.97)	1	2.00 (0.23-17.62)
Possible- exposure	54	11	1.10 (0.52-2.34)	2	0.57 (0.12-2.63)	4	0.96 (0.30-3.06)	6	6.22 (1.51-25.73)*	6	1.56 (0.56-4.34)
Non-exposure	168	31	1.00	11	1.00	13	1.00	3	1.00	12	1.00

Results from unconditional logistic regression analysis. The results are presented as OR and 95% CI.
[a] Included astrocytoma
[b] Included craniopharyngioma, trigeminal neuroma, and primary central nervous system lymphoma.
*$p < 0.05$.

developing a brain tumor. When the analyses were restricted to a histological type, the three EMF exposure levels (non-exposure, possible-exposure and explicit-exposure) showed a dose-response trend with brain tumors, particularly a significant association between acoustic neuromas and explicit-exposure as well as between gliomas and possible-exposure. Our finding of an increased risk for brain tumors corresponds with results from other studies on occupational cancer[19]. However, Johansen's study, which did not stratify by histological type, found no such relationship[20].

Nevertheless, separate analyses of brain tumors in men and women have found higher ORs in men when exposure was assessed by self-report. In contrast, a SEARCH study conducted in Germany[21], which classified exposure according to job-titles, found that a significant increased risk for brain tumor development was associated with working in electrical occupations for women but not for men. We observed a higher risk among men who may have been exposed to a wide variety of agents, some of which may be very closely correlated with EMF exposure.

Elevated risk estimates were found for acoustic neuroma and glioma when the analyses were stratified by histological type. The association between occupational exposure to EMF and meningioma or pituitary adenoma, in this study, was relatively weak (non-significant). The Nurses' Health Study cohort suggests the risk for meningioma increases among women exposed to either endogenous or exogenous sex hormones[22]. Custer showed that some hormonal exposures may influence tumor biology in women who develop meningioma[23].

The strengths of our study need to be considered in relation to many previous studies. Acoustic neuroma has recently received attention as possibly being related to cell phone use. The evidence for a link to cell phone use is somewhere between weak and negative[24]. Most of the studies reporting slight increases in risk found the effect in groups with the longest duration of use, typically at least 10 years before diagnosis[25-27]. A SEARCH study conducted in Sweden by Rodvall et al.[17] which examined occupational exposure to EMF and brain tumors showed a slightly elevated risk for glioma. Another population-based case-control study conducted in Canada, which classified exposure according to average magnetic field exposure through blinded expert review (< 0.3, 0.3-0.6, and ≥ 0.6 μT), found a significant increased risk of glioblastoma multiforme[15]. Contrary to our findings, a population-based case-control study (414 cases and 421 controls) in Australia observed no significant association in both low and high grade gliomas[28]. There are conflicting results regarding the biologic plausibility for a causal relationship between EMF and acoustic neuroma or glioma. Many laboratory studies indicate that EMF plays a role in cancer promotion with an effect on such things as signal transduction, differentiation, growth, and cell-to-cell communication[29].

There are several limitations of this study. First, our study lacks information on power frequency magnetic fields inside and outside the home. The occupational exposure to EMF should also include other surrounding exposures (exposure to mobile phone or electrical appliances) for each exposure category in that it would be more likely that the subjects true exposure was "non-exposure plus other sources", "possible-exposure plus other sources" and "explicit-exposure plus other sources", respectively. The OR value for subjects holding a "possible-exposure" job was more stable. Perhaps magnetic fields encountered in "possible-exposure" jobs do not add enough to the background exposure to increase the risk if, in fact, magnetic fields do affect risk. The OR value for the category with the highest occupational exposure was unstable, given the small number of subjects in this group (5 cases and 4 controls for males, 4 cases and 3 controls for females). This limits the interpretability of the OR value for the explicit-exposure category, though patients with metastatic brain tumors and angiomas were excluded from this study, and hence the results can improve the validity. Second, this study did not include the exposure to organic solvents because it was impossible to find out the dosage of exposure to organic solvents and workers might not be able to identify the category of organic solvents. So the research did not compare the association between exposure to organic solvents and occupational exposure to EMF in brain tumors. The participants in this study may have been exposed to a wide variety of chemicals such as solvents, lead pesticides/herbicides and petroleum products which have been shown to have an interactive effect with magnetic field exposure[30]. Information on these chemical exposures was not available for our study, so their potential effects were not considered. Finally, another limitation was the small number of subjects in the category of "explicit-exposure," which resulted in wide confidence intervals particularly in the subgroup analysis. The numbers were especially insufficient for meaningful analyses of the specific pathological cell types.

In conclusion, the results of this hospital-based case-control study support the hypothesis that an increase in occupational exposure to EMF will increase the risk of developing a brain tumor, especially in males. Additionally, the occupational EMF exposure elevates the risk of acoustic neuroma and glioma. The results of this study support the possibility that occupational EMF exposure plays a role in the etiology of brain tumors.

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Original Article

利用問卷調查職業暴露於電磁場與腦瘤及其組織病理型態之相關性探討

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目的：本研究旨在探討職業暴露到電磁場與腦瘤及其組織病理型態之間的相關性。

材料與方法：研究設計採以醫院為基礎的病例－對照研究法，於2004年9月至2005年2月募集中山醫學大學附設醫院神經外科111位腦瘤病患（病例組）及235位與電磁場暴露無關之疾病、非腦瘤之住院及門診患者（對照組），分別進行問卷訪談（個人基本資料、個人/家族疾病史、職業暴露電磁場史、抽菸習慣）。將所有受試者職業所可能暴露的電磁場分為三組：無暴露於電磁場組、可能暴露於電磁場組、明確暴露於電磁場組，並以卡方檢定及羅吉斯迴歸進行資料分析。

結果：在調整各項干擾因子後，發現男性明確暴露於電磁場者相較於無暴露於電磁場者有顯著增加罹患腦瘤的機率，其危險對比值為7.37 (95% CI: 1.36-40.03)。隨後，進一步依腦瘤的組織病理型態進行分析，結果顯示明確暴露於電磁場者相較於無暴露於電磁場者有顯著增加罹患膠質瘤的機率，其危險對比值為7.39 (95% CI: 1.91-28.54)；可能暴露於電磁場者相較於無暴露於電磁場者有顯著增加罹患聽神經瘤的機率，其危險對比值為6.22 (95% CI: 1.51-25.73)。

結論：利用問卷調查職業暴露於電磁場可能使腦瘤的危險性增加，特別是膠質瘤與聽神經瘤。

關鍵詞：腦瘤、電磁場、職業暴露、病例對照研究

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