ORIGINAL ARTICLE

Occupational exposure to power frequency magnetic fields and risk of non-Hodgkin lymphoma

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21 March 2006**Objectives:** To investigate the risk of non-Hodgkin lymphoma (NHL) using a job-exposure matrix (JEM) to assess exposure to occupational magnetic fields at the power frequencies of 50/60 Hz.**Methods:** The study population consisted of 694 cases of NHL, first diagnosed between 1 January 2000 and 31 August 2001, and 694 controls from two regions in Australia, matched by age, sex and region of residence. A detailed occupational history was given by each subject. Exposure to power frequency magnetic fields was estimated using a population-based JEM which was specifically developed in the United States to assess occupational magnetic field exposure. The cumulative exposure distribution was divided into quartiles and adjusted odds ratios were calculated using the lowest quartile as the referent group.**Results:** For the total work history, the odds ratio (OR) for workers in the upper quartile of exposure was 1.48 (95% CI 1.02 to 2.16) compared to the referent (p value for trend was 0.006). When the exposure was lagged by 5 years the OR was 1.59 (95% CI 1.07 to 2.36) (p value for trend was 0.003). Adjusting for other occupational exposures did not significantly alter the results.**Conclusions:** These findings provide weak support for the hypothesis that occupational exposure to 50/60 Hz magnetic fields increases the risk of NHL.

Non-Hodgkin lymphoma (NHL) has been one of the most rapidly increasing cancers in developed countries over the last 40 years.^{1,2} In Australia, the incidence of NHL over the last decade has risen by an average of 0.8% per year in females and by 1.7% per year in males.³ Although the causes of this rise are not clear, it has been suggested that an increase in exposure to environmental or occupational agents may be partially responsible.⁴ The generation and use of electricity has greatly increased in the past 50 years, although it is uncertain whether this has resulted in a rise in the individual exposure to power frequency (50/60 Hz) magnetic fields.⁵

Several researchers have examined the possibility that exposure to power frequency magnetic fields increases the risk of NHL. Early studies of workers found an association between NHL and electrical occupations, which were believed to have an elevated exposure to magnetic fields.^{6,7} However, the lack of individual information on level and duration of exposure weakens any causal inferences derived from these studies. Several later industry-based studies performed on electric utility workers, which assessed individual exposures, did not confirm the earlier findings.^{8–12}

We used a population-based job-exposure matrix (JEM) to assess the magnetic field exposure in a large Australian case-control study of incident NHL. Our aim was to determine whether occupational exposure to power frequency magnetic fields is associated with an increased risk of NHL.

METHODS

Information on the study population, including subject characteristics and exclusions, has been given in detail previously.¹³ Briefly, cases were patients notified to the New South Wales (NSW) Central Cancer Registry with incident NHL first diagnosed between 1 January 2000 and 31 August 2001. They had to be 20–74 years of age and reside in NSW or the Australian Capital Territory (ACT). Controls were randomly selected from the NSW and ACT electoral rolls to approximately match the expected distributions of cases with respect to age,

sex and region of residence (NSW or ACT) at diagnosis. Electoral registration is compulsory for Australian citizens aged 18 years or over. Cases were excluded if they had a history of organ transplantation or HIV infection. Cases and controls were excluded if they had poor English language skills, illness or a disability that prevented a 60-minute telephone interview. Otherwise eligible subjects who had died before initial contact or before interview for the study were also excluded from data collection. Of 842 cases approached for interview, 717 (85%) participated. Twenty three cases were subsequently excluded after a pathology report review because of low confidence in the diagnosis of NHL, leaving a total of 694 cases. Altogether, 694 of 1136 eligible and contactable controls were interviewed (61%).

An introductory letter and an information leaflet outlining the requirements of participation in a research project relating to the effects of the environment on the development of NHL were mailed to each subject; neither the letter nor the information leaflet specifically mentioned magnetic fields. Consent to participate was obtained by telephone. A self-administered questionnaire was then mailed to each subject to obtain demographic details, smoking status and other information of interest to the study. In addition, each subject completed a lifetime calendar with a detailed occupational history including each job title, employer, industry, start and finish years, number of hours worked per day and number of days worked per week. Participants were requested to only include jobs that they held for one year or more, and to record the job that they had for the longest time if they had more than one job in a particular year. Subjects also completed a 60-minute computer-assisted telephone interview about other selected occupational, environmental, immunological and infectious risk factors for NHL that are the subject of other reports.^{13–17}

Exposure to power frequency magnetic fields was estimated using a population-based JEM which was specifically developed at the University of Washington in the United States to assess

Abbreviations: JEM, job-exposure matrix; NHL, non-Hodgkin lymphoma

Table 1 Demographic characteristics of 694 non-Hodgkin lymphoma cases and 694 controls

	No of cases (n = 694)	% of cases	No of controls (n = 694)	% of controls
Age group				
Males	404	58.2	397	57.2
20–39	38	5.5	41	5.9
40–59	190	27.4	182	26.2
60–74	176	25.4	174	25.1
Females	290	41.8	297	42.8
20–39	25	3.6	26	3.7
40–59	133	19.2	127	18.3
60–74	132	19.0	144	20.7
State				
NSW	666	95.9	662	95.4
ACT	28	4.1	32	4.6
Ethnicity				
British or Irish	508	73.3	545	78.5
Asian	23	3.4	14	2.0
European	72	10.4	46	6.6
Other	91	12.9	89	12.8

occupational magnetic field exposure.¹⁸ Exposure in the JEM was based on approximately 2400 magnetic field measurements conducted during 10 studies in the United States, Sweden, New Zealand, Finland and Italy.^{19–28} The majority of the measurements (97%) came from personal exposure data although spot measurements (3%) were also used. Job titles in the JEM were assigned occupational codes which corresponded to the 1980 Standard Occupational Classifications (SOC).²⁹ The exposure metric used in the JEM was the geometric mean of the magnetic field measurements for one workday within an occupation, measured in units of microTesla (μ T).

All jobs held by each subject were allocated their relevant SOC occupational code so that the magnetic field exposure for each job could be assigned according to the exposure value given by the JEM. The coding was initially performed by a health physicist and was then checked by an industrial hygienist, both of whom had several years experience in assessing occupational magnetic field exposure. The exposure for each subject was then calculated by multiplying the duration of employment in each work history record by the corresponding entry of the JEM and aggregating across the total work history to obtain a cumulative estimate of exposure in units of “ μ T-years”. One μ T-year corresponds to a workday geometric mean exposure of 1 μ T for one calendar year.

In the analysis, we compared four levels of exposure that were calculated by dividing the cumulative exposure distribution into quartiles and using the lowest quartile as the referent group. Odds ratios (ORs) and 95% confidence intervals (95%

CI) adjusted for age, sex, state of residence and ethnic origin were derived from multivariate logistic regression models using SPSS software (SPSS Inc., Chicago, IL, USA). In addition, ORs were estimated for the cumulative exposure as a continuous variable by transforming the cumulative exposure distribution into its natural log. The possibility of confounding with other occupational exposures was considered by adjusting for wood dust, pesticides and all solvents other than benzene (aromatics, chlorinated hydrocarbons and aliphatics), which were found to be associated with NHL in other recent analyses of the subjects in this study.^{15–16} In order to account for possible latency of the effect of exposure to magnetic fields on the development of NHL, ORs and 95% CIs were also calculated for a 5-year lag period prior to diagnosis. We tested for a linear trend across quartiles of exposure using logistic regression.

The study was approved by the human research ethics committee at each participating institution. Written informed consent was obtained from each participant in the research.

RESULTS

The demographic characteristics of 694 cases of NHL and 694 controls are shown in table 1. Cases and controls were well matched by sex, age and region of residence and had similar proportions for ethnic origin. There was, however, a deficit of Asians and Europeans in the control group possibly because of a relative deficit of people of these ethnicities on the electoral roll. The main occupations for cases and controls are shown in table 2.

Table 2 Main occupations of 694 non-Hodgkin lymphoma cases and 694 controls

Job title	No of cases (n = 694)	% of cases	No of controls (n = 694)	% of controls
Sales workers	130	18.7	144	20.4
Managers and administrators	87	12.5	108	15.6
Farm workers	84	12.1	69	9.9
General office clerks	77	11.1	96	13.8
Administrative support occupations	75	10.8	61	8.8
Truck drivers	54	7.8	36	5.2
Protective service occupations	49	7.1	40	5.8
Secretaries	44	6.3	58	8.4
Nurses	44	6.3	43	6.3
Teachers	39	5.6	57	8.2

Figure 1 Distribution of the cumulative magnetic field exposure for the entire work history of 694 NHL cases and 694 controls.

Figure 1 shows the distribution of the cumulative exposure for the entire work history of all the subjects as given by the JEM. The mean cumulative exposure was 8.41 $\mu\text{T-years}$ with a range of 117.44 $\mu\text{T-years}$. The 25th, 50th and 75th centiles were 3.92, 6.31 and 9.85 $\mu\text{T-years}$, respectively. The cumulative exposure was mainly driven by the duration of exposure which had a mean of 31.7 years and a range of 71 years (the 25th, 50th and 75th centiles for the duration were 22, 33 and 42 years, respectively). The intensity of exposure had a mean of 0.26 μT and a range of 2.35 μT (the 25th, 50th and 75th centiles for the intensity were 0.16, 0.21 and 0.27 μT). With a 5-year lag, the cumulative exposures were slightly less, as expected, with a mean of 7.61 $\mu\text{T-years}$ and a range of 114.45 $\mu\text{T-years}$. The 25th, 50th and 75th centiles were 3.35, 5.62 and 9.10 $\mu\text{T-years}$, in that order.

Table 3 presents ORs for NHL relative to total and 5-year lag cumulative exposure. Both the total and 5-year lag periods had similar risk estimates with the 5-year lag period having slightly higher ORs. Although the ORs for the second quartile compared to the referent were below the null at 0.81 (95% CI 0.58 to 1.13) and 0.94 (95% CI 0.67 to 1.32) for total and 5-year lag exposure, respectively, there was a statistically significant trend of increasing risk with increasing exposure ($p = 0.006$ for total exposure and $p = 0.003$ for 5-year lag exposure). Subjects in the highest exposure group had ORs of 1.48 (95% CI 1.02 to 2.16) for total exposure, and 1.59 (95% CI 1.07 to 2.36) for the 5-year lag exposure. Modelled as a continuous variable, there was a rise in the ORs of approximately 18% and 24% per log $\mu\text{T-year}$ for the total and 5-year lag exposure, respectively.

Considering other occupational exposures, adjusting for pesticides, wood dust and all solvents other than benzene did not significantly alter the results with the ORs being slightly lower (table 3). Subjects in the highest exposure group, when adjusting for these exposures, had ORs of 1.33 (95% CI 0.90 to 1.96) for total exposure, and 1.43 (95% CI 1.07 to 2.36) for the 5-year lag exposure (corresponding p values for trend were 0.034 and 0.018). As a continuous variable, the ORs increased by approximately 14% and 19% per log $\mu\text{T-year}$ for the total and 5-year lag exposure, respectively.

DISCUSSION

In this study we investigated the relationship between occupational exposure to power frequency magnetic fields and the risk of developing NHL, by applying a job-exposure matrix in the assessment of magnetic field exposure. We also

examined separately the magnitude of the association for exposures received by subjects for their entire work history and 5 years prior to the date of diagnosis. Our results provide support for a weak positive association between occupational exposure to 50/60 Hz magnetic fields and NHL. For the total cumulative exposure period there was a rise in the strength of the association to reach the highest risk estimates in the upper quartile of exposure.

Lagging the exposure period by 5 years showed a similar rise in the risk with increasing exposure that produced statistically significant associations in the third and upper quartiles of exposure, respectively. The 5-year lag, generally increased the ORs slightly and this could reflect an aetiological process with a delay between early exposure and a late-stage effect.³⁰ Two previous studies on occupational magnetic fields and NHL that examined lag periods have shown contradictory results. In a study conducted at five electric utility companies in the USA, a slightly stronger association was shown for past exposures between 10 and 20 years.¹¹ However, a study conducted more recently at the Ontario Hydro in Canada reported a weaker association with a 10-year lag and a further decrease in the risk with a 20-year lag.¹²

A major strength of the present study was the use of a JEM which was specifically designed to assess exposure to power frequency magnetic fields. However, the JEM was based on measurements performed in countries outside Australia and, although large differences are not expected, the possibility of variation in the measurements for the same job titles in Australia remains.

The component of magnetic fields that may be relevant to biological effects remains uncertain. If the true risk factor was not the cumulative exposure, as used in this study, but some other index relevant to magnetic fields (such as peak or intermittent exposures), additional misclassification would result. However, other indices (peaks, time above threshold, etc) have been shown to be quite closely correlated to the mean magnetic field strength, suggesting that the cumulative exposure is a good surrogate for the true metric.⁹ In addition, the JEMs used in this study differ from previous work in that historical changes in exposure were not taken into account. Our inability to adjust for changes in exposure over time may have increased exposure misclassification, which limits the detection of associations with other metrics.

Despite the limitations in assessing magnetic field exposure, there is no reason to suppose that errors in estimating exposure are differential between cases and controls. This should mainly lead to non-differential misclassification and bias the risk estimates towards the null, particularly for the very high exposure group.³¹

Other strengths of this study include the large number of cases and controls, the fact that the study was population-based, the use of incident cases rather than deaths, and the fact that participation, especially for cases, was acceptable. However, some cases not included were too ill to be interviewed or died before they could be recruited into the study. Therefore, cases with more aggressive NHL are more likely to be under-represented in our study population. Another limitation was the possibility of recruitment bias among the controls with regard to ethnic origin due to the use of the electoral roll as a sampling frame and, possibly, less participation from people of non-English speaking background. Although approximately 16% of cases were not on the electoral roll, there was no substantial change in the results when excluding these cases from the analysis. There was a lack of controls from Asian and European backgrounds and, although ethnicity was included as a covariate in all models of the analysis, there may be residual confounding if there is an association between ethnic origin and exposure to magnetic fields.

Table 3 Risk of non-Hodgkin lymphoma relative to total and 5-year lag cumulative magnetic field exposure

	Cumulative magnetic field exposure (μ T-years)	No of cases	No of controls	OR*	(95% CI)*	OR†	(95% CI) †
Total exposure							
1st quartile	<3.92	170	177	1.00		1.00	
2nd quartile	3.92–<6.31	150	197	0.81	0.58 to 1.13	0.80	0.57 to 1.11
3rd quartile	6.31–<9.85	185	162	1.34	0.94 to 1.92	1.29	0.90 to 1.86
4th quartile	≥ 9.85	189	158	1.48	1.02 to 2.16	1.33	0.90 to 1.96
Continuous (log μ T-year)				1.18	1.00 to 1.40	1.14	0.96 to 1.35
5-year lag exposure							
1st quartile	<3.36	165	182	1.00		1.00	
2nd quartile	3.36–<5.63	154	193	0.94	0.67 to 1.32	0.92	0.66 to 1.29
3rd quartile	5.63–<9.11	191	156	1.61	1.12 to 2.33	1.53	1.06 to 2.22
4th quartile	≥ 9.11	184	163	1.59	1.07 to 2.36	1.43	0.96 to 2.14
Continuous (log μ T-year)				1.24	1.05 to 1.46	1.19	1.01 to 1.41

*Odds ratios (OR) and associated 95% confidence intervals (95% CI) adjusted for age, sex, state of residence and ethnic origin; p for trend was 0.006 and 0.003 for total and 5-year lag exposure respectively.

†Odds ratios (OR) and associated 95% confidence intervals (95% CI) adjusted for age, sex, state of residence, ethnic origin, solvents other than benzene (aromatics, chlorinated hydrocarbons and aliphatics), wood dust and pesticides; p for trend was 0.034 and 0.018 for total and 5-year lag exposure respectively

Unlike other environmental agents, electric and magnetic fields are present in all environments where electric power is used. The potential effects of electric fields as well as non-occupational exposures to magnetic fields were not considered in this study and this may have introduced confounding or effect modification.¹¹ Only one occupational study has evaluated the relation between electric fields and NHL, which has suggested in two separate analyses a twofold and threefold risk, respectively, in the Ontario Hydro cohort.^{10–12} For non-occupational magnetic fields, the relatively few studies have mainly concentrated on children and, in general, have shown a lack of an association between residential exposures and NHL.^{32–34}

There is a paucity of information on possible risk factors associated with NHL, so uncontrolled confounding cannot be ruled out.¹¹ The strongest known risk factors for NHL are immunodeficiency and specific viral infections, but these exposures are not expected to be associated with exposure to magnetic fields.⁴

The subjects in this study may have been exposed to a wide variety of agents, some of which may be very closely correlated with magnetic field exposure within a given industry. Occupations such as farmers, woodworkers, and workers in various metal industries have been associated with NHL.² A recent analysis of the subjects in this study examined the relationship between the risk of NHL and occupational exposure to solvents, metals, organic dusts, polychlorinated biphenyls (PCBs) and pesticides.^{15–16} The risk of NHL was increased by about 30% with a dose-response relationship for all solvents other than benzene. Exposure to wood dust also

increased the risk of NHL slightly. Exposures to other organic dusts, metals and PCBs were not strongly related to NHL. Exposure to substantial doses of all types of pesticides tripled the risk of NHL. We addressed the possibility of confounding between magnetic field exposure and occupational exposure to pesticides, wood dust and all solvents other than benzene in our analyses and found little evidence of it.

In terms of lifestyle factors, although information was collected on cigarette smoking and socioeconomic status, these variables were not included in the analysis. Previous analyses of the same data showed a lack of an association between NHL and smoking; this is consistent with several large cohort and case-control studies.¹³ An earlier investigation of sun exposure and NHL using the data of this study did not find an appreciable difference in socioeconomic status between cases and controls and its inclusion in that analysis had no effect.¹⁴

Our results provide support for a weak positive association between occupational power frequency magnetic fields and NHL, particularly at high levels of exposure. The underlying mechanisms for such an association, if causal, are still unclear. Further experimental studies are needed on the specific biological effects, if any, of magnetic fields.

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Competing interests: None.

Main messages

- In a large case-control study, the application of a job-exposure matrix showed a weak positive association between occupational power frequency magnetic fields and risk of non-Hodgkin lymphoma, particularly at high levels of exposure.
- Adjusting for other occupational risk factors did not significantly alter the results.

Policy implications

- Further occupational studies employing various methods of exposure assessment are required to confirm these findings.

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