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Occupational exposure to extremely low-frequency magnetic fields and electrical shocks and acute myeloid leukemia in four Nordic countries

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Abstract
Objective We studied the association between occupational exposure to extremely low-frequency magnetic fields (ELF-MF) and electrical shocks and acute myeloid leukemia (AML) in the Nordic Occupational Cancer cohort (NOCCA).
Methods We included 5,409 adult AML cases diagnosed between 1961 and 2005 in Finland, Iceland, Norway, and Sweden and 27,045 controls matched by age, sex, and country. Lifetime occupational ELF-MF exposure and risk of electrical shocks were assigned to jobs reported in the censuses using job-exposure matrices. We estimated hazard ratios (HRs) and 95 % confidence intervals (95 % CIs) using conditional logistic regression adjusted for concurrent occupational exposures relevant for AML risk (e.g., benzene, ionizing radiation). We conducted sensitivity analyses with different assumptions to assess the robustness of our results.

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Results Approximately 40 % of the subjects were ever occupationally exposed to low levels and 7 % to high levels of ELF-MF, whereas 18 % were ever at low risk and 15 % at high risk of electrical shocks. We did not observe an association between occupational exposure to neither ELF-MF nor electrical shocks and AML. The HR was 0.88 (95 % CI 0.77–1.01) for subjects with high levels of ELF-MF exposure and 0.94 (95 % CI 0.85–1.05) for subjects with high risk of electrical shocks as compared to those with background-level exposure. Results remained materially unchanged in sensitivity analyses with different assumptions.
Conclusion Our results do not support an association between occupational ELF-MF or electric shock exposure and AML.

Keywords Extremely low-frequency magnetic fields · Electrical shocks · Acute myeloid leukemia · Nordic countries · Case–control study · Job-exposure matrix

Introduction

Acute myeloid leukemia (AML) has been linked to a number of environmental and occupational factors. Of these, ionizing radiation and benzene are the most established risk factors for adult AML [1–4]. Other suspected environmental factors include pesticides, solvents, formaldehyde, and electric and magnetic fields among others [5–7].

The evidence for an association between extremely low-frequency magnetic fields (ELF-MF) and AML is inconsistent. Several studies have shown positive associations with occupational exposure [7–11], while others reported no associations [12–15]. Reasons for these inconsistent results are unknown, but could be due to differences in exposure assessment, study populations, and low number of exposed cases. Recently, an update of a previously used job-exposure matrix (JEM) to assess occupational ELF-MF exposure was published and subsequently used in a prospective study on occupational ELF-MF and cancer in the Netherlands [7]. This study reported an increased risk of adult AML associated with exposure to ELF-MF. The study was, however, limited due to a relatively small number of exposed AML cases. In addition, since high occupational exposure to ELF-MF is correlated with the risk of electrical shocks [16] and other occupational exposures, it is necessary to disentangle the potential effects of ELF-MF from those of other exposures. Therefore, the present study extends the previous analyses using the population-based Nordic Occupational Cancer cohort (NOCCA) to assess the association between occupational exposure to ELF-MF, occupational risk of electrical shocks, and AML.

Methods

The current study is a case–control study nested within the NOCCA cohort. The NOCCA cohort includes 14.9 million adults from Finland, Iceland, Norway, Denmark, and Sweden who participated in at least one of the population censuses in 1960, 1970, 1980/1981, and/or 1990. The NOCCA cohort has been previously described in detail by Pukkala et al. [17]. We did not have access to individual-level data for Denmark, and therefore, Danish data are not included in the current analyses. Follow-up of the cohort was established by linkage between national population and cancer registries for information on cancer, death, and emigration.

All incidence adult AML cases (codes C92.0 + C93.0 + C94.0 + C94.2 + C94.4–5 in the 10th version of International Classification of Diseases, ICD-10) diagnosed from 1961 to 2005 who did not have a previous history of cancer were included in this study. Five controls, alive and who did not have a history of cancer on the date of diagnosis of the case (hereafter the "index date"), were randomly selected from the NOCCA cohort. Controls were matched to each case by year of birth, sex, and country. Study participants were at least 20 years old at the index date and had occupational information from at least one census. Because of larger uncertainties in the exposure estimates to ELF-MF and other occupational exposures before the Second World War, we included in the main analyses only those subjects who started their employment career after 1945.

Information on occupation was available from censuses 1960, 1970, 1980, and 1990 in Sweden; from 1960, 1970, and 1980 in Norway; and from 1970, 1980, and 1990 in Finland. In Iceland, the only computerized census available was from 1981. Census questionnaires were self-administered and included questions related to the respondents' economic activity, occupation, and industry. They were filled in by the heads of household for all members of the household in Finland, Norway, and Sweden, whereas each individual of at least 17 years old filled them out in Iceland. Validity studies indicated reasonably high accuracy in occupational classification based on census records in Nordic countries [18–21]. In Finland, Norway, and

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Sweden, occupation was coded according to national adaptations of the Nordic Occupational Classification (NYK), a Nordic adaptation of the International Standard Classification of Occupations (ISCO) from 1958 [22]. In Iceland, occupation was coded according to a national adaptation of ISCO-68 [23]. A conversion was made to NYK in order to homogenize the occupational codes of the four countries.

Occupational exposure to ELF-MF and risk of electrical shocks were assigned to each subject based on census-reported jobs using job-exposure matrices [7, 16]. Since these JEMs were based on ISCO-88 job codes, we first translated the NYK codes into ISCO-68 using an automated crosswalk developed in the INTEROCC Project and subsequently into ISCO-88 using an existing automated crosswalk [24]. Because the coding systems are similar, these translations do not lead to a large change in occupational exposure assignments due to one-to-many and many-to-one code translation [25]. Ordinal ELF-MF and electric shock exposure levels were assigned to each census job (i.e., background, low and high exposure) by linking the JEM to the coded job histories.

We used three exposure metrics for ELF-MF and electrical shocks: (1) ever exposure to low and/or high levels; (2) duration (in years) of ever low/high and ever high exposure; and (3) cumulative exposure. Cumulative exposure was calculated by multiplying the duration of the job with an arbitrary assigned weight to the exposure rating reflecting the multiplicative nature of the exposure distribution (i.e., background 0, low 1, high 4) and expressed in unit-years [16, 26–28]. Employment period was assumed to start at age 20 years and end at either the index date or age 60 years whichever came first. If a given person had different occupations during his/her employment career, we assumed he/she changed occupation in the middle of the two censuses. Values for censuses with missing occupational codes were imputed from the nearest available census records. For Iceland, we assumed that the persons were in the same occupation as in 1981 census for the entire employment period. Cumulative exposures were categorized by using the tertiles of the exposure distribution among controls as cutoff points. We also defined electric/electronic occupations based on two previous classifications [29, 30] and used two exposure metrics for them: (1) ever/never exposed and (2) duration (in years) of ever exposed.

Participants classified as economically inactive (i.e., no paid jobs reported) were assigned to background levels of ELF-MF and risk of electrical shocks and not involved in electrical/electronic occupations.

We quantified concurrent occupational exposures previously associated with AML risk (benzene, toluene, trichloroethylene, methylene chloride, aliphatic and alicyclic hydrocarbon solvents, 1,1,1-tetrachloroethylene, formaldehyde, and ionizing radiation) through linkage with the NOCCA job-exposure matrix (NOCCA-JEM). The NOCCA-JEM covers over 300 specific occupations; 29 exposure factors; and 4 periods: 1945–1959, 1960–1974, 1975–1984, and 1985–1994 [31]. Exposure factors in NOCCA-JEM are characterized by the proportion of exposed (P) and mean level of exposure (L) in a specific job and time period. We assigned the product of the proportion and level of exposure (P $\times$ L) of the selected exposures to each job and then multiplied this by employment period in years to derive cumulative estimates. This procedure was the same as described previously in Talibov et al. [32].

In this study, we present the distribution of occupational exposure to ELF-MF, occupational risk to electrical shocks, and working in an electric/electronic occupation for the total sample, by case–control status, and by sex. As the risk estimates the incidence of AML, we used conditional logistic regression models to estimate hazard ratios (HRs) and 95 % confidence intervals (95 % CIs). All models were adjusted for concurrent occupational exposures on a continuous scale. We also performed test for trend to assess exposure–response relationship between ELF-MF, electrical shocks, and AML.

We conducted several sensitivity analyses to assess the robustness of our results. To assess the effect of lag time on our results, we performed analyses with 0-, 5-, 10-year lag time. To allow for different exposure windows accounting for the uncertainty in retirement age, we estimated career duration and exposures from age 20 to 60 and 20 to 65 years. Because Icelandic data ($n = 684$, 0.85 %) was based on only 1981 census records, we also performed sensitivity analyses by excluding Icelandic data and limiting analyses to the 1980 census information in all countries. Finally, because the main analysis included economically inactive persons ($n = 4{,}931$, 6.1 %), we performed analyses with economically inactive persons excluded.

Results

Distribution of cases and controls by exposures of interest is shown in Table 1. Altogether, 13,435 persons were diagnosed with AML between 1961 and 2005 in Finland, Iceland, Norway, and Sweden. Of these, we included in the main analysis 5,409 cases and 27,045 matched controls who started their employment after 1945. Approximately 40 % percent of the subjects were ever exposed to low and 7 % to high levels of ELF-MF, whereas 18 % were ever at low and 15 % at high risk of electrical shocks. The numbers and proportions of males in higher exposure categories were considerably larger than those of females for all

Table 1 Distributions of occupational extremely low-frequency magnetic fields, electrical shock exposures, and electric/electronic occupations for cases and controls

Agent	Male				Female				Total			
	Cases		Controls		Cases		Controls		Cases		Controls	
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Total	2,917	100	14,585	100	2,492	100	12,460	100	5,409	100	27,045	100
Extremely low-frequency magnetic fields												
Ever exposed to												
Background levels	1,475	50.6	7,094	48.6	1,398	56.1	6,733	54.0	2,873	53.1	13,827	51.1
Low levels	1,090	37.4	5,608	38.5	1,075	43.1	5,599	44.9	2,165	40.0	11,207	41.4
High levels	352	12.1	1,883	12.9	19	0.8	128	1.0	371	6.9	2,011	7.4
Cumulative exposure[a]												
0 unit-years	1,475	50.6	7,094	48.6	1,398	56.1	6,733	54.0	2,873	53.1	13,827	51.1
1–16.2 unit-years	425	14.6	2,235	15.3	566	22.7	2,997	24.1	991	18.3	5,232	19.3
16.2–29.9 unit-years	405	13.9	2,003	13.7	366	14.7	1,829	14.7	771	14.3	3,832	14.2
29.9–159.9 unit-years	612	21.0	3,253	22.3	162	6.5	901	7.2	774	14.3	4,154	15.4
Electrical shocks												
Ever exposed to												
Background levels	1,571	53.9	7,672	52.60	2,055	82.5	10,010	80.3	3,626	67.0	17,682	65.4
Low levels	582	20.0	3,008	20.6	398	16.0	2,218	17.8	980	18.1	5,226	19.3
High levels	764	26.2	3,905	26.8	39	1.6	232	1.9	803	14.8	4,137	15.3
Cumulative exposure[a]												
0 unit-years	1,571	53.9	7,672	52.6	2,055	82.5	10,010	80.3	3,626	67.0	17,682	65.4
1–19.9 unit-years	321	11.0	1,829	12.5	286	11.5	1,649	13.2	607	11.20	3,478	12.9
19.9–45.7 unit-years	424	14.5	2,108	14.5	125	5.0	678	5.4	549	10.1	2,786	10.3
45.7–159.9 unit-years	601	20.6	2,976	20.4	26	1.0	123	1.0	627	11.6	3,099	11.5
Electric/electronic occupations												
Ever exposed (yes vs. no)[b]	281	9.6	1,404	9.6	37	1.5	185	1.5	318	5.9	1,589	5.9
Ever exposed (yes vs. no)[c]	144	4.9	742	5.1	28	1.1	144	1.2	172	3.2	886	3.3

[a] Tertiles of exposure distribution among exposed controls used as cutoff points

[b] Classification based on Deapen and Henderson 1986 [29]

[c] Classification based on Feychting et al. 2003 [30]

exposure factors. For example, approximately 12 % of males and only 1 % of females were ever occupationally exposed to high ELF-MF levels.

We did not observe any statistically significant associations between ELF-MF, electrical shock, electric/electronic occupation, and AML risk in this study (HR = 0.88, 95 % CI 0.77–1.01 for those subjects with high levels of ELF-MF exposure compared to those with background levels; HR = 0.94, 95 % CI 0.85–1.05 for those subjects with high risk of electrical shocks compared to those with a background risk) (Tables 2, 3, 4). Analysis stratified by sex showed largely consistent result with no significant associations between ELF-MF, electrical shock, electric/electronic occupation, and AML risk.

Our results did not materially change in sensitivity analyses with different assumptions.

Discussion

The results of this large population-based study did not provide support for an increased risk of AML associated with occupational exposure to ELF-MF, electrical shocks, or being employed in electric/electronic occupation.

The main limitation of our study is the inevitable potential for exposure misclassification, which may arise from two sources. First, job-exposure matrices cannot account for inter-individual differences in exposure within jobs [33, 34]. Second, because work history data in our study were based on census records of jobs held by individuals at the time of census, we did not necessarily know about each change of occupation during the entire working career and had to make some assumptions on duration of employment in the exposure assignment. Of note, we did

Table 2 Hazard ratios (HRs) and 95 % confidence intervals (95 % CIs) of occupational exposure to low-frequency magnetic fields and acute myeloid leukemia

Agent	Male			Female			Total		
	HR	95 % CI	*p* for trend	HR	95 % CI	*p* for trend	HR	95 % CI	*p* for trend
Ever exposed to									
Background levels	1.00		0.09	1.00		0.08	1.00		0.02
Low levels	0.95	0.86–1.04		0.93	0.85–1.02		0.94	0.88–1.00	
High levels	0.89	0.76–1.03		0.75	0.45–1.23		0.88	0.77–1.01	
Duration of ever low/high exposed (HR/10 years)[a]	0.99	0.96–1.03		0.99	0.95–1.03		0.99	0.97–1.02	
Duration of ever high exposed (HR/10 years)[a]	0.99	0.93–1.05		0.91	0.66–1.26		0.99	0.93–1.05	
Cumulative exposure[b]									
Background (0 unit-years)	1.00		0.20	1.00		0.16	1.00		0.06
1–16.2 unit-years	0.91	0.81–1.04		0.92	0.82–1.03		0.92	0.84–0.99	
16.2–29.9 unit-years	0.99	0.87–1.12		0.97	0.85–1.11		0.98	0.89–1.08	
29.9–159.9 unit-years	0.95	0.81–1.03		0.88	0.73–1.06		0.91	0.82–0.99	

[a] The risk associated with 10-year increase in duration of exposure

[b] Tertiles of exposure distribution among exposed controls used as cutoff points

Table 3 Hazard ratios (HRs) and 95 % confidence intervals (95 % CIs) of occupational exposure to electrical shocks and acute myeloid leukemia

Agent	Male			Female			Total		
	HR	95 % CI	*p* for trend	HR	95 % CI	*p* for trend	HR	95 % CI	*p* for trend
Ever exposed to									
Background levels	1.00		0.35	1.00		0.03	1.00		0.08
Low levels	0.95	0.85–1.06		0.88	0.78–0.99		0.92	0.85–0.99	
High levels	0.95	0.85–1.07		0.81	0.49–1.31		0.94	0.85–1.05	
Duration of ever low/high exposed (HR/10 years)[a]	1.00	0.97–1.04		0.99	0.93–1.05		0.99	0.97–1.03	
Duration of ever high exposed (HR/10 years)[a]	0.99	0.96–1.04		1.03	0.78–1.34		1.00	0.96–1.04	
Cumulative exposure[b]									
Background (0 unit-years)	1.00		0.96	1.00		0.13	1.00		0.52
1–19.9 unit-years	0.85	0.74-0.98		0.86	0.75-0.98		0.86	0.78-0.94	
19.9–45.7 unit-years	0.99	0.87-1.12		0.92	0.75-1.13		0.97	0.87-1.08	
45.7–159.9 unit-years	0.99	0.88–1.12		1.14	0.67–1.94		1.00	0.89–1.12	

[a] The risk associated with 10-year increase in duration of exposure

[b] Tertiles of exposure distribution among exposed controls used as cutoff points

observe associations between some of the known occupational risk factors, notably benzene, and AML risk which would indicate that the uncertainty in job duration is not a major limitation (data not shown).

The large study population, accurate case ascertainment, and complete cancer and mortality follow-up history for all non-emigrating study participants are evident advantages of this study. Finally, by using a previously further improved ELF-MF JEM and a previously developed electrical shock JEM, we were able to look comprehensively at ELF-MF exposure by assessing not only exposure to magnetic fields but also potential for electrical shocks and employment in an electrical occupation.

Previous studies have provided only modest support for a possible association between magnetic field exposure and AML. Kheifets et al. [35] published a meta-analyses based

Table 4 Hazard ratios (HRs) and 95 % confidence intervals (95 % CIs) of electric/electronic occupations and acute myeloid leukemia

Agent	Male		Female		Total	
	HR	95 % CI	HR	95 % CI	HR	95 % CI
Classification based on Deapen and Henderson [29]						
Ever exposed (yes vs. no)	1.01	0.87–1.17	1.09	0.68–1.76	1.02	0.88–1.17
Duration of ever exposed (HR/10 years)[a]	1.04	0.98–1.11	1.22	0.93–1.59	1.05	0.99–1.11
Classification based on Feychting et al. [30]						
Ever exposed (yes vs. no)	0.96	0.79–1.17	1.06	0.61–1.86	0.98	0.81–1.18
Duration of ever exposed (HR/10 years)[a]	1.00	0.92–1.09	1.16	0.84–1.61	1.02	0.94–1.10

[a] The risk associated with 10-year increase in duration of exposure

on studies up to 2007 and reported a positive association between occupational ELF-MF exposure and AML (pooled relative risk 1.16, 95 % CI 1.11–1.22). Interestingly, increased risks were mainly seen in the older studies, while newer studies only showed a marginal increase in risk albeit that test for heterogeneity was non-significant. The recent prospective Netherlands Cohort Study [7] also reported a modest statistically significantly increased risk of AML following exposure to ELF-MF. Using the same job-exposure matrix as in the latter study, we did not confirm such an association for ELF-MF in our study with considerably larger number of AML cases. Additional analyses stratified by sex and country did not alter this observation. As such the evidence base linking ELF-MF with AML risk remains weak.

In conclusion, the results of this study did not provide further support for an association between occupational ELF-MF exposure, risk of electrical shocks, and AML incidence.

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Ethical standard This research was based on the Nordic Occupational Cancer cohort (NOCCA) study data, which was created through the linkage of readily available information from various types of registries. No direct contact was needed with study subjects. Therefore, ethical committee statement was not required for the implementation of this study.

Conflict of interest The authors declare no conflict of interest in connection with this article.

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