Occupational Exposure to Electric Shocks and Magnetic Fields and Amyotrophic Lateral Sclerosis in Sweden

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Background: Amyotrophic lateral sclerosis (ALS) has been consistently related to "electric occupations," but associations with magnetic field levels were generally weaker than those with electrical occupations. Exposure to electric shock has been suggested as a possible explanation. Furthermore, studies were generally based on mortality or prevalence of ALS, and studies often had limited statistical power.

Methods: Using two electric shock and three magnetic field job-exposure matrices, we evaluated the relationship of occupational magnetic fields, electric shocks, electric occupations, and incident ALS in a large population-based nested case–control study in Sweden. Subanalyses, specified a priori, were performed for subjects by gender and by age (less than and more than 65 years).

Results: Overall, we did not observe any associations between occupational magnetic field or electric shock exposure and ALS. For individuals less than 65 years old, high electric shock exposure was associated with an odds ratio (OR) of 1.22 (95% confidence interval [CI] = 1.03, 1.43). The corresponding result for the age group 65 years or older was OR = 0.92 (95% CI = 0.81, 1.05). Results were similar regardless which job exposure matrices, exposure definitions, or cutpoints were used. For electric occupations, ORs were close to unity, regardless of age. For welders, no association was observed overall, although for welders <65 years the OR was 1.52 (95% CI = 1.05, 2.21).

Conclusions: In this very large population-based study based on incident ALS case subjects, we did not confirm previous observations of higher risk of ALS in electrical occupations, and provided only weak support for associations between electric shocks and ALS.

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Amyotrophic lateral sclerosis (ALS), part of a family of motor neuron diseases, is a fatal, incurable disease striking nerve cells in the brain and the spinal cord. This rapidly progressive neurodegenerative disease has a worldwide incidence rate of 1.2 to 2.5/100,000 per year, peaking around 70 years old and affecting people between 40 and 75 years of age.[1–3] Etiologic mechanisms in ALS remain elusive. Approximately 5% of ALS cases are familial,[4] suggesting that environmental exposures may play an important role in the occurrence of ALS. There are, however, no established environmental or occupational risk factors for ALS, although the evidence for smoking is suggestive.[5] In the epidemiologic literature, ALS has been associated with "electric occupations."[6,7] Within electric occupations, welders have been of particular interest, but results have been inconsistent, with some studies finding an association,[8] while others did not.[9] In addition to the complex electromagnetic field environment, with fields ranging from static to high frequency,[10] welders are coexposed to neurotoxic agents.[11]

Magnetic fields, electric fields, contact currents, microshocks, and both perceptible and imperceptible electric shocks all contribute to the extremely low-frequency electromagnetic field environment in occupational settings. Numerous studies have evaluated extremely low-frequency magnetic fields as a risk factor, but reported associations with magnetic field levels are generally weaker than those in electrical occupations[6,7] Exposure to electric shock has been suggested as a possible explanation, but until recently, occupational studies could not address exposure to electric shocks, either as a risk factor or a confounder.[7,12,13] Two recent ALS studies have examined both electric shock and magnetic field exposure. One found no support for either electric shocks or magnetic fields as an explanation for the association between electric occupations and ALS,[9,14] while the other study found some evidence of an association with magnetic fields, but not with electric shocks or electric occupations.[15]

A previous study of the employed Swedish population examined the association between electrical occupations, including welding and other occupations exposed to magnetic fields, and ALS mortality.[8] We expand on this study by focusing on incident ALS cases, extending time periods of study and follow-up, and adding information on electric shock exposure. Using two electric shock and three magnetic field job-exposure matrices, we evaluated the relationship of occupational magnetic fields, electric shocks, electric occupations, and ALS in a registry-based nested case–control study in Sweden. The availability of multiple job-exposure matrices for each exposure measure allowed us to perform sensitivity analyses to evaluate potential dependence on the choice of job exposure matrices.

METHODS

Study Base

The study population comprises individuals born in Sweden from 1901 to 1970 and included in the 1990 Swedish Population and Household Census. Via the National Registration Numbers, a unique identifier for residents of Sweden, we followed the study population via linkages to the Swedish Patient Register, Migration Register, and Cause of Death Register between January 1, 1991, and December 31, 2010.

The Swedish Patient Register collects information on all hospitalizations since 1964/1965 (nationwide complete since 1987) and >80% clinic visits to specialist outpatient care since 2001. Information recorded includes the dates of admission and discharge as well as discharge diagnoses, coded according to the Swedish revisions of the *International Classification of Diseases* (ICD): ICD-9 from 1987 to 1996 and ICD-10 from 1997 to present. Follow-up of the study population was censored at first ALS diagnosis, migration out of Sweden, or death, whichever came first.

The study was approved by the Regional Ethical Review Board in Stockholm, Sweden.

Case and Control Subjects

Within the study base, we conducted a nested case–control study. We defined ALS cases as those with a discharge record of either an inpatient or outpatient clinic visit in the Patient Register with ALS as the underlying or a secondary diagnosis (ICD-9: 335C and ICD-10: G12.2). Date of first ALS diagnosis was defined as the case index date. Using incidence density sampling, we randomly selected five control subjects per ALS case subject from the study base, individually matched by birth year and sex. Control subjects had to be alive, living in Sweden, and have no diagnosis of ALS as of the case index date.

Potential Confounders

Highest educational level obtained at the index date was retrieved from the Swedish Education Register and was categorized as 9 years, 12 years, or university education. Socioeconomic status (SES) based on occupational position as of last available census in 1980 or 1990 was coded as White Collar, Blue Collar, Farmers, Self Employed, and Unclassified/Missing. Since the unclassified or missing SES constituted 13% of the study population, these were included in the analysis as a separate category and excluded as part of a sensitivity analysis. Region of residence was used with categories: north/middle/south according to the 1990 Census.

Magnetic Field Exposure

The primary magnetic field job-exposure matrix (MF-JEM) used in this analysis is an extension of the INTEROCC JEM,[16] and updated with occupational measurements from the 1000 Person Study,[17] which provided the most complete coverage of occupations. As secondary MF-JEMs, we combined two job-exposure matrices utilizing Swedish exposure data developed by Floderus for men and Forssén for women.[18,19] When available, we used gender-specific estimates; otherwise the only available estimate was used for both men and women. The Swedish MF JEMs have a slightly higher number of missing observations (2%). The geometric mean of full-shift, time-weighted-averages of the magnetic flux density in micro-Tesla (μT) by job was used to describe magnetic field exposure in both job-exposure matrices. Another secondary MF-JEM was a modified version of a MF-JEM,[20] in which the original exposure intensities categorized into low-, medium-, and high-magnetic field levels based on distributional cut points at 0.15 and 0.30μT, were subsequently up- or downgraded by two industrial hygienists based on the estimated probability of exposure per job.[21]

Using a priori cutoffs at 0.15 and 0.30 μT, the modified INTEROCC and Swedish job exposure matrices were categorized into low, medium, and high exposures. Sensitivity analyses included examination of cutpoints (<0.11, 0.12–0.19, 0.20–0.29, and >0.3 μT) from previous studies based on the Swedish MF-JEM.[8]

Electric Shocks Exposure

The primary electric shock job-exposure matrix (ES-JEM) was a European ES-JEM, based on injury data obtained from five European countries, and the number of workers per occupation and country from EUROSTAT. Accident rates were pooled across countries with a random effects model and categorized jobs into low, medium, and high electric shock risk based on the 75th and 90th percentile of the pooled accident rates distribution.[21] For sensitivity analyses, we used a US ES-JEM in which exposure is defined as the percent of workers ever exposed to electric shocks during their working life. Exposures were derived from expert elicitation using a combination of injury and electrocution data and expert occupational knowledge. The US ES-JEM includes estimates for the median percentage of workers exposed to electric shocks by occupation.[14,22] Coded as 1990 US Bureau of Census codes, the job-exposure matrix was converted to four-digit ISCO88 by an experienced industrial hygienist (Vergara et al. 2015 in preparation) and categorized into low, medium, and high risk based on the 75th and 90th percentiles of the estimated median exposure prevalence to make it comparable with the European ES-JEM.

Electrical Occupations

We defined electrical occupations as in Deapen and Henderson (1986), translated into 13 Swedish codes (Table 1 footnote).

Occupational Coding

We linked the case and control subjects to the censuses to ascertain individual occupations coded at three-digit level 1980 Swedish codes. We converted the job-exposure matrices coded in three- or four-digit level ISCO88 codes to three-digit 1980 Swedish codes using a previously established crosswalk developed for the Nordic Occupational Cancer Study (NOCCA, 2014). The crosswalk was checked by an industrial hygienist (PW) familiar with both codes. In addition, jobs not converted in the crosswalk (n = 4) were manually coded by the industrial hygienist. Our analysis is the subset of case and control subjects employed for at least one of the 1960, 1970, 1980, or 1990 censuses. If a case subject was excluded because of missing exposure data, the corresponding matched control subjects were also removed.

Exposure Classification

The primary analyses considered the highest exposure in one's working career identified from any of the four censuses. If a subject never worked in a high exposure occupation, but worked in a "medium" exposure occupation for at least one occupational census, he/she was assigned a "medium" exposure. All others were assigned "low" exposure used as the reference group.

As a crude assessment of duration of exposure, we also compared those with high exposure in three or more censuses, to those with lower exposures or high exposure in two or fewer censuses. In addition, we calculated cumulative exposure by multiplying the continuous exposure assignments (if available, if not we used exposure weights of low: 0, medium: 1, and high: 4) by the duration of each job and summed these products over the calendar period covered by the censuses for each person. Calculations of job duration assumed a working age between 20 and 65 years. Jobs recorded in each census continued to the midpoints of the censuses and extended beyond the 1960 and 1990 census as long as the individual was within his/her working lifetime.[23] The most recent adjacent census information filled in missing census information when necessary. The proportion with missing information varied between censuses from 0.8% (1960) to 3.7% (1990), and did not differ materially between case and control subjects, or between age groups. High-, medium-, and low-cumulative exposures were categorized by the 75th and 90th percentiles of the resulting distribution among controls. Supplementary data, eTable 1A (http://links.lww.com/EDE/A957) gives further details about the job-exposure matrices used in this analysis.

TABLE 1. Description of Overall Dataset

	Case Subjects (N = 4,709)	Control Subjects (N = 23,335)
	No. (%)	No. (%)
Age		
<65 years old	1,660 (35)	8,310 (36)
≥65 years old	3,049 (65)	15,025 (64)
Gender		
Male	2,775 (59)	13,783 (59)
Female	1,934 (41)	9,552 (41)
Education		
≤9 years	2,129 (45)	10,904 (47)
10–12 years	1,698 (36)	8,145 (35)
University	798 (17)	3,805 (16)
Missing	84 (2)	481 (2)
SES		
White collar	1,761 (37)	8,941 (38)
Blue collar	1,914 (41)	9,185 (39)
Farmers	165 (4)	845 (4)
Self-employed	293 (6)	1,316 (6)
Unclassified/missing	576 (12)	3,048 (13)
Region		
North	1,064 (23)	5,191 (22)
Middle	2,512 (53)	12,480 (54)
South	1,133 (24)	5,664 (24)
Occupation type		
Electric occupations[a]	766 (16)	3,943 (17)
Welders	77 (2)	349 (2)

[a]Includes: electrical, electronics and telecommunications engineers and technicians; railway engine drivers and assistants; motor-vehicle drivers and tram drivers; precision-tool makers; watchmakers; non-specified precision-tool manufacturing work; machinery fitters and machine assemblers; welders and flame cutters; electrical fitters and wiremen; radio and television assemblers and repairmen; recording, sound and light equipment operators; telephone and telegraph installers and repairmen; and non-specified electrical and electronics work.

SES, socioeconomic status.

TABLE 2. Ever-exposed Results for Primary Job-exposure Matrices for Full Dataset and Age Subgroups

	No. Exposed		Unadjusted for Other Exposure	Adjusted for Other Exposure
	Case Subjects	Control Subjects	OR[a] (95% CI)	OR[a] (95% CI)
Full dataset				
MF low exposure	2,272	11,229	1.00 (reference)	1.00 (reference)
MF med exposure	1,938	9,418	1.01 (0.94–1.09)	1.00 (0.93–1.08)
MF high exposure	499	2,688	0.93 (0.83–1.04)	0.92 (0.82–1.04)
ES low exposure	2,888	14,268	1.00 (reference)	1 (reference)
ES med exposure	924	4,536	1.03 (0.94–1.12)	1.03 (0.94–1.13)
ES high exposure	897	4,531	1.01 (0.92–1.11)	1.02 (0.92–1.13)
Less than 65 years				
MF low exposure	793	4,018	1.00 (reference)	1.00 (reference)
MF med exposure	682	3,418	1.01 (0.90–1.14)	0.95 (0.84–1.08)
MF high exposure	185	874	1.06 (0.88–1.28)	1.00 (0.82–1.21)
ES low exposure	950	5,019	1.00 (reference)	1 (reference)
ES med exposure	327	1,515	1.18 (1.01–1.36)	1.20 ((1.02–1.40)
ES high exposure	383	1,776	1.20 (1.03–1.40)	1.22 (1.03–1.43)
Greater than or equal to 65 years				
MF low exposure	1,479	7,211	1.00 (reference)	1.00 (reference)
MF med exposure	1,256	6,000	1.01 (0.93–1.11)	1.03 (0.94–1.14)
MF high exposure	314	1,814	0.87 (0.76–1.00)	0.89 (0.77–1.02)
ES low exposure	1,938	9,249	1.00 (reference)	1 (reference)
ES med exposure	597	3,021	0.96 ((0.87–1.07)	0.95 (0.84–1.06)
ES high exposure	514	2,755	0.92 (0.81–1.04)	0.92 (0.81–1.05)

[a]Matched on birth year, sex, and adjusted for socioeconomic status, education, and region of residence.
MF, magnetic fields; ES, electric fields.

Statistical Analyses

We developed and agreed on an analysis plan before the analysis. To aid in the interpretation of numerous possible exposure definitions and categorizations, the analysis plan specified a priori the primary and secondary job-exposure matrices to be used, based on the relevance and completeness of available exposure data in the Swedish dataset, and cutpoints to characterize exposure. We used conditional logistic regression modeling to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) adjusted for SES, highest level of education, and region of Sweden. Sub-analyses, specified a priori, were performed for subjects by gender and by age at diagnosis (and corresponding date for the matched controls) less than and over 65 years of age, since 65 is the retirement age in Sweden. Separate analyses were conducted for welders and for other electric occupations, for comparability with previous research.

RESULTS

We identified a total of 5,020 ALS cases and initially selected 25,100 controls for the analysis. Only case and control subjects employed during at least one census were included in the analysis, leaving 4,709 case subjects and 23,335 control subjects. Table 1 contains a description and distribution of the full dataset.

The results from the analysis using the primary job-exposure matrices are shown in Table 2 for the full dataset, as well as for the age subgroups. The ORs were insensitive to adjustment for the other exposure among all subgroups.

Overall, no association was observed between occupational magnetic field or electric shock exposure and ALS. For individuals less than 65 years of age, medium- and high-electric shock exposures were associated with ORs of 1.20 (95% CI = 1.02, 1.40) and 1.22 (95% CI = 1.03, 1.43), respectively, when adjusted for magnetic field exposure. For individuals ≥65 years old, the OR for high-electric shock exposure was slightly reduced (OR = 0.92; 95% CI = 0.81, 1.05); a slight reduction was also observed for high magnetic field exposure. Exposures do not appear to be confounding each other as results do not vary much depending on whether electric shocks and magnetic fields are specified in the same regression, or separately.

Associations for individuals in electric occupations (which include welders) and welders separately are shown in Table 3. For electric occupations, ORs were close to unity, regardless of age. For welders less than 65 years old, an OR of 1.52 (95% CI = 1.05, 2.21) was observed. There were no associations with other individual electrical occupations (not shown). There were also no observed associations between ALS and the

TABLE 3. Associations with Electric Occupations and Welders for Entire Dataset and Age Subgroups

	No. Exposed		
	Case Subjects	Control Subjects	OR[a] (95% CI)
Full dataset			
Electric occupations	766	3,943	0.99 (0.90–1.09)
Welders	77	349	1.16 (0.90–1.50)
Individuals younger than 65 years			
Electric occupations	324	1,581	1.05 (0.91–1.22)
Welders	38	131	1.52 (1.05–2.21)
Individuals 65 years of age or older			
Electric occupations	442	2,362	0.95 (0.84–1.07)
Welders	39	218	0.95 (0.67–1.34)

[a]Matched on birth year and sex, and adjusted for socioeconomic status, education, and region of residence.

number of times one has worked in an electric occupation or the number of times one was a welder (not shown).

Sensitivity analyses using the alternate cutpoints, demonstrate consistency with the results presented above (not shown), as did exclusion of subjects with unclassified or missing SES and analyses for the male and female subgroups (data not shown).

Results of sensitivity analyses using secondary magnetic field and electric shock job-exposure matrices are consistent with the analysis based on primary job-exposure matrices (Supplementary Data, eTable 2A, 3A, 4A; http://links.lww.com/EDE/A957). Supplementary Data, eTable 5A (http://links.lww.com/EDE/A957) presents exposure distributions as percent of case and control subjects for the primary- and secondary-job exposure matrices. Most occupations with low-magnetic field exposure tend to have low exposure to electric shocks, and occupations with medium- and high-magnetic field exposure vary between all electric shocks exposure categories, with some variation between job-exposure matrices.

Because we observed an elevated OR for ALS among welders, we excluded welders and repeated the analyses using primary MF-JEM and ES-JEM. We observed similar (but slightly weaker) ORs associated with electric shocks (Supplementary Data, eTable 6A; http://links.lww.com/EDE/A957).

Timing of Exposure

To determine whether the timing of the exposure was a factor in the association with ALS, we examined people exposed in both the 1980 and 1990 censuses, those exposed in either 1980 or 1990, and those not exposed in either year (reference) (Supplementary Data, eTable 7A; http://links.lww.com/EDE/A957).

For those younger than 65 years, exposure in 1980 seems to be driving the association with ALS, although the OR is still slightly raised for those exposed in 1990 but not 1980. There does also not appear to be an association with magnetic fields in any of the subgroups and no association with electric shock for those 65 years or older.

Finally, although based on limited occupational history data, we also examined cumulative exposure effects. Cumulative results are roughly consistent with the results based on highest exposed occupation: no associations are observed for the group as a whole, while a raised OR is observed for electric shock exposure for individuals less than 65 years old (Supplementary Data, eTable 8A; http://links.lww.com/EDE/A957). Similar OR point estimates were observed for number of censuses with exposure to high magnetic fields or electric shocks for the overall dataset and age group subsets; however, CIs were wider and overlapped the null for all estimates (not shown).

DISCUSSION

In this large, population-based study of incident cases of ALS, we found no association overall between ALS and magnetic fields or electric shock exposure, and no evidence that electric shock was a confounder in the analyses of magnetic fields, as has been hypothesized.[7] Our results indicate that the working population less than 65 years old, with high or medium occupational exposure to electric shocks, may have a slightly higher risk of ALS. Our results were similar regardless which job-exposure matrices, exposure definitions, or cutpoints were used.

While we did not see any relationship between ALS and electric occupations, we found an increased risk of ALS among welders, but only restricted to those less than 65 years. However, we still observed a raised OR associated with electric shock exposure in this age group after excluding welders; thus, they do not explain the observed relationship between ALS and electric shock exposure.

This study has several strengths. In addition to the large sample size, population-based exposure and outcome information, and prospectively collected information on occupations, an important advantage compared with previous studies is the use of incident ALS case subjects instead of cause of death data or small clinic-based samples of prevalent case subjects. Use of both electric shocks and magnetic field job exposure matrices, with sufficient number of discordant exposures, allowed us to examine these exposures separately and together, which has been done only in two studies previously. Another unique advantage of this study is its use of multiple job exposure matrices to measure electric shock and magnetic field exposure, which enhances comparability with previous studies, and allows us to check for consistency.

However, we did not have access to a full occupational history, and could not control for other potential confounders, such as smoking, alcohol consumption, physical activity, and other occupational exposures. A recent ALS study from the Netherlands reported a high to moderate correlation between occupational exposures to magnetic fields, electric shocks, solvents and metals, but these exposures did not confound the results.[24] Another potential limitation is that the Swedish patient register through which ALS subjects were identified only included inpatient visits until 2000, while specialist outpatient visits were included from 2001 onwards, i.e., the last 10 years of our study period. It is therefore likely that during the early period, we may have missed case subjects who had not been hospitalized either specifically for ALS or for other reasons with ALS as a secondary diagnosis. However, inclusion of patients from the outpatient register from 2001 should allow us to capture most, if not all, case subjects since ALS patients often need to visit a specialist for a definitive diagnosis and treatment. Furthermore, in a previous study, we observed that patients in the inpatient register were hospitalized with a mean of 5 months after first outpatient identification which suggests that even the inpatient register might have identified ALS case subjects in a timely manner.[25] During the study period, the disease classification for ALS changed from ICD9 (covering the period through 1996) to ICD10 (1997 onwards). The ICD9 code 335C is specific to ALS, whereas the ICD10 code G12.2 includes all motor neuron diseases, of which ALS comprises more than 90%.[26]

There are several possible explanations for a higher risk in the younger age group. Exposure misclassification might be reduced when restricting to age groups that have not yet retired. Older persons (65 years or more) may be considered retired in the most recent censuses, and may be classified as unexposed even if they had been exposed before the first available census. In addition, their cumulative exposure will be lower for the same reason. There is also a possibility that timing of exposure is critical, if electric shocks are of importance mainly for early onset ALS. We found some evidence that exposure in the 1980s conferred higher risk, although the OR was still slightly raised for those exposed in 1990 but not 1980. An alternative explanation is random variation, especially considering that some of the ORs in the older age group were slightly reduced.

Our results differ from the two previous studies that examined electric shock and magnetic field exposures jointly,[9,15] but these two studies were also not consistent. Both studies used ALS mortality as outcome. Occupational information was collected from death certificates in the US study, and from two censuses in the Swiss study. The Swiss study found no associations with electric occupations or electric shocks, and a moderately increased risk of ALS associated with magnetic field exposure.[15] The latter was restricted to the subgroup with medium/high exposure in two consecutive censuses (46 case subjects), with no consistent risk increase by intensity of exposure in the overall analysis, where the risk estimate was raised for medium exposure but not for the highest exposure. The number of exposed case subjects was small, however, and the point estimates for electric shock exposure were of the same magnitude as we found in the subgroup below 65 years old, although with wide CIs. The US study found no association with electric shock or magnetic field exposure,[9] while an increased risk was observed in relation to electric occupations. Examination of age-specific results revealed that the latter was restricted to the subgroup below 65 years old.

Earlier studies, which mainly focused on electromagnetic fields, have consistently found an increased risk of ALS associated with "electric occupations," but not with magnetic fields.[7] Many of these studies were, however, limited by the use of occupational and outcome information from death certificates and limited control of confounding, or were based on small numbers of case subjects occurring among workers in the utility industry. Two clinically-based studies included prevalent ALS case subjects, and control subjects were not population based,[12,27] while the only previous population-based study with incident case subjects was very small (four cases in electricity work).[28] The latter study found no association with electric shock assessed through questionnaires.

In conclusion, our large population-based study with incident ALS case subjects and exposure assessment based on multiple job-exposure matrices did not confirm previous observations of higher risk of ALS in electrical occupations or with occupational magnetic fields, and provided only weak support for electric shocks in ALS etiology. Additional studies need to be performed to clarify the relationship among ALS, electric shocks, and magnetic fields.

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