Occupational Exposure to Electric Shocks and Extremely Low-Frequency Magnetic Fields and Motor Neurone Disease

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Running head: Exposure to Electric Shocks, ELF-MF and MND

ABSTRACT

In a New Zealand population-based case-control study we assessed associations

with occupational exposure to electric shocks, extremely low-frequency magnetic fields

(ELF-MF) and motor neurone disease using job-exposure matrices to assess exposure.

Participants were recruited between 2013 and 2016. Associations with ever/never,

duration, and cumulative exposure were assessed using logistic regression adjusted for

age, sex, ethnicity, socioeconomic status, education, smoking, alcohol consumption,

sports, head or spine injury and solvents, and mutually adjusted for the other exposure.

All analyses were repeated stratified by sex. An elevated risk was observed for having

ever worked in a job with potential for electric shocks (odds ratio (OR)=1.35, 95%

confidence interval (CI): 0.98, 1.86), with the strongest association for the highest level

of exposure (OR=2.01, 95%CI: 1.31, 3.09). Analysis by duration suggested a non-linear

association: risk was increased for both short-duration (<3 years) (OR= 4.69, 95%CI:

2.25, 9.77) and long-duration in a job with high level of electric shock exposure (>24

years; OR=1.88; 95%CI: 1.05, 3.36), with less pronounced associations for intermediate

durations. No association with ELF-MF was found. Our findings provide support for an

association between occupational exposure to electric shocks and motor neurone disease

but did not show associations with exposure to work-related ELF-MF.

2

electric shocks; extremely low-frequency magnetic fields; job exposure matrix; motor

neurone disease; occupational exposure; population-based case-control study

Abbreviations: ALS, Amyotrophic Lateral Sclerosis; CI, confidence interval; ELF-MF,

extremely low-frequency magnetic fields; JEM, job exposure matrix; MND, motor

neurone disease; OR, odds ratio.

Motor neurone diseases (MND) are a group of progressive, terminal neurodegenerative

conditions for which there is no cure. Amyotrophic Lateral Sclerosis (ALS) is the most

common form, accounting for 85% of cases, with other forms including Progressive

Muscular Atrophy, Progressive Bulbar Palsy and Primary Lateral Sclerosis (1). Several

environmental and occupational exposures have been associated with MND, but the

only established risk factors to date are older age, male sex, military service, and a

family history of MND (2). An association with work in "electrical occupations" has

been observed in a number of studies (3-8), with exposure to both extremely low-

frequency magnetic fields (ELF-MF) and electric shocks suggested as risk factors (9-

12). Exposure to ELF-MF and electric shocks have been considered in a number of

studies with different designs, but findings have been inconsistent, with some showing

positive associations with electric shocks (13, 14), whereas no association was found in

other studies (3, 15, 16). Similarly, occupational exposure to ELF-MF was associated

with MND in some studies (17-19) but not in others (20, 21).

The few studies that investigated both exposures within the same study, using

job-exposure-matrices (JEMs), have also provided conflicting findings (5, 22-25). In

particular, a US case-control study, using only the main occupation registered on death

certificates to assess exposure, found a weak positive association with ELF-MF, but an

inverse association with electric shocks (23). In addition, a Swedish population-based

case-control study found no association between exposure to ELF-MF and ALS, while

3

an association with electric shocks was observed, but only in people aged <65 years (5).

Also, cohort studies from the Netherlands and Switzerland, both with incomplete job

histories, showed an increased risk of ALS with ELF-MF, but not electric shocks (24,

25). However, the most recent study, using pooled data from three European case-

control studies with life-time job histories, showed that both ever exposure to ELF-MF

and ever exposure to the potential for electric shocks above background level were

associated with ALS (22).

We have previously reported that both electricians and telecommunication

technicians (among other occupations) had elevated risks of MND (26), and have now

assessed associations with occupational exposure to ELF-MF and potential for electric

shocks using JEMs applied to lifetime occupational histories.

METHODS

Study population

As reported previously (26), the study population consisted of 396 incident and

prevalent cases with a diagnosis of MND. Cases were recruited primarily through the

MND Association of New Zealand register over a period of three years (2013-2016),

supplemented with searches (2013-2015) of the National Minimum Dataset, which

holds records of all hospital outpatients, for individuals with a primary or secondary

diagnosis of MND (ICD 10 code – G122) (27). The inclusion criterion for cases was a

diagnosis by a neurologist, including all forms of MND. Controls were randomly

selected from the New Zealand Electoral Roll (2008), two per case, frequency matched

by age (based on the age-distribution of the United Kingdom MND incidence

distribution) (28) and sex. Controls with any other neurodegenerative disease such as

Parkinson's and Alzheimer's disease were excluded based on their response to the

4

questionnaire, as these diseases can affect memory and cognition, and may also be related to occupational exposure of ELF-MF (21).

Participation rates were 92% for cases (n=321) and 48% for controls (n=605). All participants gave written informed consent. Ethics approval was provided by the Multi-region Ethics Committee in New Zealand (MEC/12/01/005).

Data collection

Data on demographic and personal characteristics, family history, lifestyle factors, and a lifetime occupational history were collected using questionnaires as described previously (26). All jobs were assigned a New Zealand Standard Classification of Occupations 1999 (29) five-digit code and the industry was coded according to the Australian and New Zealand Standard Industrial Classification 1996 (30).

Exposure assessment

We applied JEMs for potential for electric shocks (31) and ELF-MF exposure (32). The electric shocks JEM was developed by Huss et al., (31) based on pooled national accident registry data from five European countries and reflects the potential for electric injury for each three-digit code of the International Standard Classification of Occupation 1988. This JEM categorized jobs into low (background), medium and high potential for electric injury.

The ELF-MF JEM was developed in The Netherlands (32) as a modified version of the JEM developed by Bowman et al., (33) based on magnetic fields measurements taken on or near workers from 10 studies in the United States, Sweden, New Zealand, Finland, and Italy. It reflects both intensity and probability of exposure to magnetic flux

5

density for each job (the 4-digit code of International Standard Classification of Occupation 1988) on a scale of low (background), medium and high. The median intensity of these magnetic field categories were 0.11µT for background, 0.19 µT for low and 0.52 µT for high exposure.

In order to apply the JEMs, occupations of study participants were re-coded from New Zealand Standard Classification of Occupations 1999 to International Standard Classification of Occupation 1988 using a correspondence table.

Participants who ever had a job with exposure above background level were considered as exposed; those who never worked in an occupation with exposure above background level served as the reference category.

Duration of exposure was defined as the number of years with exposures above background level. Cumulative exposure was expressed as unit-years, which was calculated as the product of the level of exposure (using arbitrary units 0 for background, 1 for medium and 4 for high level/probability of exposure, as used in previous studies (22, 24)), and duration in years for each exposed job, summed over the entire job history. The cut-points for categories of duration and cumulative exposure were based on the quartiles of exposure in the controls (22).

The exposure metrics developed for ELF-MF included: (1) ever/never exposure above background level; (2) level of exposure (background; medium exposure only; ever high exposure); (3) duration of exposure (background; <3 years; 3-8; 9-23; >23 years); and (4) cumulative exposure (background; <4 unit years; 4-12; 13-28; >28 unit years).

The exposure metrics developed for electric shocks included: (1) ever/never exposure above background level; (2) level of exposure (background; medium exposure only; ever high exposure); (3) duration of exposure (background; <3 years; 3-8; 9-24;

6

>24 years); and (4) cumulative exposure (background; <4 unit years; 4-16; 17-52; >52 unit years).

Statistical analyses

Analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina). Differences in general characteristics between cases and controls were tested using Chi-squared tests, and unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

ORs were reported with adjustment for age (5-year categories) and sex. The 'fully adjusted' ORs were also adjusted for ethnicity (European, Māori, Pacific & others); highest achieved education level (primary and secondary school, technical or trade school diploma, undergraduate university degree, postgraduate university degree); smoking status before diagnosis (never, ex, smoker at the time of diagnosis); alcohol consumption before diagnosis (≤once a month,1-2 times/week, 3-5 times/week, daily); sports (never versus ever in adulthood (>18 years); head injury (never/ever); spine injury (never/ever); and socioeconomic status using the New Zealand Deprivation Index 2006 (quintiles) (34). Models were also adjusted for self-reported occupational exposure (never/ever) to solvents using a detailed questionnaire, and mutually adjusted for ELF-MF or electric shocks. All analyses were repeated separately for males and females.

We also explored the effects of additional adjustments for other self-reported occupational exposures, including fumes, gas, dust, fibers, acids or alkalis, fumigants, fungicides, insecticides, herbicides or timber preservatives, other chemical products, animals or animal products. Analyses were also stratified by age (<65, ≥65).

Categorical variables for duration of exposure and cumulative exposure were used in regression models, again using background level as the reference. A test for

7

trend was performed by fitting these categorical exposure variables as a continuous variable.

Latency analyses were conducted with employment 5, 10, 20 and 40 years prior to the interview date disregarded. Participants without employment during the lag time were excluded from these analyses.

RESULTS

Population characteristics

A total of 319 cases and 604 controls were included in the analyses (Table 1), two cases and one control without occupational history were excluded. Most cases (67% male and 69% female) were aged >60 years. While the 70+ age group was overrepresented in the controls, there was little difference between cases and controls in terms of tobacco smoking, ethnicity, and education. However, there was a difference in socioeconomic status for males, with cases less deprived compared to controls. There was no difference in the number of occupations held (mean=6.8 for cases and controls).

Potential exposure to electric shocks

The results on potential exposure to electric shocks are presented in Table 2. Among cases, 55% had ever worked in occupations with potential exposure to electric shocks above background level (44% in controls), and 32% had ever worked in an occupation with high potential for exposure to electric shocks (19% in controls). An elevated risk was found for potential exposure to electric shocks above background (OR 1.35, 95% CI: 0.98,1.86) in both males and females (OR males 1.35, 95%CI: 0.87, 2.10; OR females 1.38, 95%CI: 0.80, 2.35, respectively, Web Tables 1 and 2). Similarly, we observed an increased risk for high potential exposure to electric shocks (OR 2.01,

8

95%CI: 1.31, 3.09), also in both males and females (OR 1.83, 95%CI: 1.11, 3.02, and OR 6.88, 95%CI: 1.13, 42.12, respectively, Web Tables 1 and 2), although for women, employment in a job with high potential for electric shock was rare.

Analysis by duration of employment in a job with potential for electric shocks showed a significantly elevated risk for short durations (<3 years) (OR 1.85, 95%CI: 1.18, 2.90), particularly for those who had a job with high potential for electric shock (OR 4.69, 95%CI: 2.25, 9.77). More than 24 years of duration in jobs with high potential for electric injury was also associated with an increased risk (OR 1.88, 95%CI: 1.05, 3.36).

For cumulative exposure, a similar pattern of elevated risks in the lowest and highest categories was observed, but this did not reach statistical significance when adjusted for all potential confounders. In females, a statistically significant positive trend was observed for cumulative exposure (p-test for trend=0.02), with the highest risk shown for the 17-52 unit-years exposure category (OR 4.02, 95%CI: 1.25, 12.92, Web Table 2).

When we repeated the analyses using 5, 10, 20 and 40 years lag, the risk estimates changed only slightly from 5 years (OR=1.45) to 20 years lag time (OR=1.50), with a small drop for the 40 years lag time (OR=1.42) (Table 3).

Exposure to ELF-MF

The prevalence of occupational exposure to ELF-MF above background was 59% for cases and 62% for controls, and 9% of cases ever had high exposure compared with 8% of controls (Table 4). No association between exposure to ELF-MF and MND was observed and ORs did not increase with longer duration or higher cumulative exposure (Table 4, Web Tables 3 and 4).

9

Cumulative exposure to ELF-MF and electric shocks were moderately correlated (Pearson correlation: R=0.32, p<0.0001). The effect of ELF-MF adjustment on the association between potential exposure to electric shocks and MND was small, as was the effect of adjustment for solvent exposure. For example, the OR for ever exposed to the highest level of electric shocks changed from 1.89 to 2.04 when adjusted for ELF-MF, and from 2.04 to 2.01 when also adjusting for solvent exposure (other data not shown).

The effect of adjustment for potential for electric shocks and solvents on the association between exposure to ELF-MF and MND was also small. For example, the OR for ever exposed to the highest level of ELF-MF changed from 0.80 to 0.73 after adjustment for electric shocks and from 0.73 to 0.71 after additional adjustment for solvents (other data not shown). Additional adjustment for other occupational exposures (see methods) did not change the results for both electric shocks and ELF-MF (data not shown).

Analyses stratified by age at interview (<65 versus ≥65 years) showed that potential for electric shocks was associated with MND in both age groups. However, associations were more pronounced for those <65 years. For example, the OR for exposure to the highest level of electric shocks was 3.32 (95%CI: 1.60, 5.92) in the younger age group, compared to 1.43 (95%CI: 0.73, 2.81) in the older age group (other data not shown).

DISCUSSION

In this study, we found a statistically significant increased risk of MND associated with employment in jobs with a high potential for electric shocks. No association was observed for ELF-MF.

10

The increased risk associated with electric shocks reported here is consistent with earlier studies (3, 11, 14, 35-38). A recent study similar to ours, which assessed the potential for electric shocks with lifetime occupational history using JEMs, also reported positive associations (22). However, other studies that assessed the potential for electric shocks through JEMs (5, 23-25), most with access to the only occupation recorded on the census (5, 25) or death certificates (23), showed less consistent results.

We found that MND was associated with employment in occupations with a high potential for electric shocks (OR 2.01; 95%CI: 1.31, 3.09), while in those with medium potential it was not, suggestive of a dose-response association. The association was observed in both men and women and risk estimates did not change after adjusting for other potential risk factors including exposure to ELF-MF and solvents. Confounding is therefore an unlikely explanation of the findings, although confounding by an, as yet, unidentified occupational risk factor present in electrical occupations cannot be excluded.

We observed a non-linear duration-response association for exposure to potential electric shock, similar to that reported in another case-control study that used the same JEM (22). This suggests that the potential for electric shock may be higher in short duration jobs (<3 years), during which workers have not yet gained the experience to prevent such risks (39); this is consistent with earlier suggestions that young electricians may be more likely to experience electric shocks (40). The observed increased risk for long (>24 years) employment in jobs with high electric shock potential may be explained by accumulated mild electric injury due to multiple (minor) shocks over longer periods, but also by a higher chance of a single large electric shock when employment duration is longer. To further explore (non-linear) dose-response associations with duration of exposure to electric shocks, we also applied generalized

11

additive modeling with spline smoothing function (GAM in SAS 9.4). Similar to the

categorical analyses (Table 2), this analysis showed elevated ORs particularly for the

short duration of potential exposure to electric shocks (results not presented).

Our latency analyses suggest there may be a long lag, of potentially several

decades, between electrical injury and disease onset as, even when disregarding

employment periods that occurred up to 20-40 years prior to diagnosis, the association

with electric shock potential remained. However, studies into severe electrical injuries

(e.g. lightning), where the timing of the one-off injury was known, have suggested a

short interval (median 2.25 years) between the electrical injury and disease onset (40).

A causal mechanism to explain the association between electric shocks and

MND has not been established. A recent review (41) suggested that electrical current

may hyper-stimulate glutamatergic neurons which can lead to free radical formation

through oxidative stress, which may either gradually break down endothelial vascular

cells, cutting off blood supply and ending in the death of spinal neurons, or directly

damage myelin, gradually leading to a demyelinating neurodegenerative condition

without vascular involvement (42, 43). Electric shock could also result in heat-

denatured proteins (44) leading to protein folding problems, which may form a

productive misfolded protein seed that could propagate to non-injured regions (45).

Thus, while an association between electric injury and MND is plausible and has

been observed in multiple studies, the epidemiological evidence remains inconsistent,

possibly due to shortcomings in the assessment of exposure to electric shocks. Some

studies have relied on self-reports of electric shock, which could result in recall bias and

false-positive findings (40). Most studies, like this study, relied on a JEM, which is less

sensitive to recall bias, but cannot indicate if or when an electric injury occurred (as it

12

only estimates the potential for electric shock), resulting in non-differential exposure misclassification and resultant potential attenuation of risk estimates (46).

We did not observe an association between ever exposed to ELF-MF above background and MND, and ORs did not increase with longer duration or higher cumulative exposure. In additional analyses, we applied another ELF-MF JEM (47) (an enhanced JEM based on the original JEM described by Bowman et al. (33)) developed as part of the INTEROCC study (47). These resulted in an OR for ELF-MF above background of 1.12 (95%CI: 0.80, 1.57; Web Table 5), and ORs did not increase with longer duration or higher cumulative exposure. For females, there was a suggestion of a positive dose-response association, however, this did not reach statistical significance (p-value for trend for duration 0.16 and for cumulative exposure 0.13, Web Table 5).

Our findings for ELF-MF are not consistent with a recent systematic review (48), which reported a meta-estimate of 1.89 (95%CI: 1.31, 2.73) for the category of highest-longest occupational exposure to ELF-MF based on six studies (7, 24, 49-52) that used full occupational histories to assess exposure to ELF-MF via JEM. An MND case-control study (22) published since the 2018 systematic review (48), which used a full occupational history similar to our study and the modified Bowman JEM (32), reported a similar OR for ELF-MF above the background level of 1.10 (95%CI: 0.95, 1.28) after adjustment for other exposures, also without a clear dose-response association.

Thus, although a recent systematic review supports the hypothesis that ELF-MF may be a risk factor for MND, our study does not, marking the need for more research in this area.

This study is limited by the relatively small size and some limitations in exposure assessment, as noted above. Another limitation was that the JEMs used in the

13

current study were not based on New Zealand exposure data, although the ELF-MF JEM did use New Zealand specific data for its construction among data from four other countries (33). The electric shocks JEM was based on data from several European countries, rather than being from any specific country (31). While there is no indication that New Zealand's occupation-specific exposure levels to ELF-MF and electric shocks are substantially different from those of European countries, we cannot exclude the possibility this has resulted in exposure misclassification. The age distribution also differed between cases and controls, for both men and women. This is likely due to age matching of controls using the age distribution of MND incidence in the United Kingdom, as equivalent New Zealand data was not available at the time of participant recruitment. However, all associations were adjusted for age. Most previous studies assessed associations between ELF-MF or electric shocks with ALS, while in this study all forms of MND were included (MND subtype specific diagnosis was not recorded), which is a limitation. However, ALS is the most common form of MND accounting for 85% of the total cases, and our case definition is therefore unlikely to differ substantially from those used in other studies on ELF-MF or potential electric shocks.

This study has several strengths, including the use of JEMs combined with full lifetime occupational histories collected without the use of proxies, which is likely to have limited recall bias. Also, cases and controls reported the same number of jobs (mean=6.8), and the number of jobs held by cases and controls was not different by age group (mean=7 for both <60 years of age and 60-70 years age group; mean=6 for 70+ years age group) suggesting that there was no indication of differential recall in occupational history between cases and controls. Furthermore, we were able to adjust the analyses for potential confounders by collecting extensive information on education,

14

socioeconomic status, smoking, alcohol consumption, and injury, as well as other (self-reported) occupational exposures.

Case ascertainment is a significant challenge when studying neurodegenerative disease (53). Our use of the MND Association of New Zealand register and the National Minimum Dataset to identify MND cases is a strength, and our association with MND Association of New Zealand resulted in a high case participation rate (92%). The participation rate among population controls was lower (48%), but we compared the occupations as recorded on the Electoral Roll between participating and non-participating controls, which showed no difference in frequency of digit 3 job codes for occupations particularly relevant for the exposures of interest, e .g. Building Finishers and Related Trades workers (0.83% in non-participating versus 0.66% in participating controls) and Electricians (0.56% in non-participating versus 0.50% in participating controls; data not show). It is therefore unlikely that the increased risks observed for potential exposure to electric shocks in this study are explained by non-response bias.

In conclusion, this study supports earlier findings that occupational exposure to electric shocks is associated with an increased risk of MND. Associations were observed in both men and women and were strongest for employment in jobs with the highest potential for electric shock. Occupational exposure to ELF-MF was not associated with the risk of MND in this study.

REFERENCES

1.   National Amyotrophic Lateral Sclerosis (ALS) Registry, Centers for Disease
        Control and Prevention, US Department of Health & Human Services. What is
        Amyotrophic lateral sclerosis (ALS)? .
        https://www.cdc.gov/als/WhatisAmyotrophiclateralsclerosis.html. Published
        2018. Updated April 6, 2018. Accessed December 10, 2019.
2.   Armon C. An Evidence-Based Medicine Approach to the Evaluation of the Role
        of Exogenous Risk Factors in Sporadic Amyotrophic Lateral Sclerosis.
        Neuroepidemiology 2003;22(4):217-28.
3.   Gunnarsson LG, Bodin L, Soderfeldt B, et al. A case-control study of motor
        neurone disease: its relation to heritability, and occupational exposures,
        particularly to solvents. *Br J Ind Med* 1992;49(11):791-8.
4.   Feychting M, Jonsson F, Pedersen NL, et al. Occupational magnetic field
        exposure and neurodegenerative disease. *Epidemiology* 2003;14(4):413-9;
        discussion 27-8.
5.   Fischer H, Kheifets L, Huss A, et al. Occupational exposure to electric shocks
        and magnetic fields and amyotrophic lateral sclerosis in Sweden. *Epidemiology*
        2015;26(6):824-30.
6.   Gunnarsson LG, Lindberg G, Soderfeldt B, et al. Amyotrophic lateral sclerosis
        in Sweden in relation to occupation. *Acta Neurol Scand* 1991;83(6):394-8.
7.   Davanipour Z, Sobel E, Bowman JD, et al. Amyotrophic lateral sclerosis and
        occupational exposure to electromagnetic fields. *Bioelectromagnetics*
        1997;18(1):28-35.
8.   McGuire V, Longstreth WT, Jr., Nelson LM, et al. Occupational exposures and
        amyotrophic lateral sclerosis. A population-based case-control study. *Am J
        Epidemiol* 1997;145(12):1076-88.
9.   Kheifets L, Bowman JD, Checkoway H, et al. Future needs of occupational
        epidemiology of extremely low frequency electric and magnetic fields: review
        and recommendations. *Occup Environ Med* 2009;66(2):72-80.
10.   Farrell DF, Starr A. Delayed neurological sequelae of electrical injuries.
        Neurology 1968;18(6):601-6.
11.   Deapen DM, Henderson BE. A case-control study of amyotrophic lateral
        sclerosis. *Am J Epidemiol* 1986;123(5):790-9.
12.   Grell K, Meersohn A, Schüz J, et al. Risk of neurological diseases among
        survivors of electric shocks: A nationwide cohort study, Denmark, 1968–2008.
        Bioelectromagnetics 2012;33(6):459-65.
13.   Filippini T, Fiore M, Tesauro M, et al. Clinical and Lifestyle Factors and Risk of
        Amyotrophic Lateral Sclerosis: A Population-Based Case-Control Study.
        International journal of environmental research and public health
        2020;17(3):857.
14.   Johansen C, Olsen J. Mortality from amyotrophic lateral sclerosis, other chronic
        disorders, and electric shocks among utility workers. *Am J Epidemiol*
        1998;148(4):362-8.
15.   Chancellor AM, Slattery JM, Fraser H, et al. Risk factors for motor neuron
        disease: a case-control study based on patients from the Scottish Motor Neuron
        Disease Register. *J Neurol Neurosurg Psychiatry* 1993;56(11):1200-6.
16.   Cruz DC, Nelson LM, McGuire V, et al. Physical trauma and family history of
        neurodegenerative diseases in amyotrophic lateral sclerosis: a population-based
        case-control study. *Neuroepidemiology* 1999;18(2):101-10.

17. Hakansson N, Gustavsson P, Johansen C, et al. Neurodegenerative diseases in welders and other workers exposed to high levels of magnetic fields. *Epidemiology* 2003;14(4):420-6; discussion 7-8.

18. Li CY, Sung FC. Association between occupational exposure to power frequency electromagnetic fields and amyotrophic lateral sclerosis: a review. *Am J Ind Med* 2003;43(2):212-20.

19. Zhou H, Chen G, Chen C, et al. Association between extremely low-frequency electromagnetic fields occupations and amyotrophic lateral sclerosis: a meta-analysis. *PLoS One* 2012;7(11):e48354.

20. Noonan CW, Reif JS, Yost M, et al. Occupational exposure to magnetic fields in case-referent studies of neurodegenerative diseases. *Scandinavian journal of work, environment & health* 2002;28(1):42-8.

21. Vergara X, Kheifets L, Greenland S, et al. Occupational exposure to extremely low-frequency magnetic fields and neurodegenerative disease: a meta-analysis. *J Occup Environ Med* 2013;55(2):135-46.

22. Peters S, Visser AE, D'Ovidio F, et al. Associations of Electric Shock and Extremely Low-Frequency Magnetic Field Exposure With the Risk of Amyotrophic Lateral Sclerosis. *Am J Epidemiol* 2019;188(4):796-805.

23. Vergara X, Mezei G, Kheifets L. Case-control study of occupational exposure to electric shocks and magnetic fields and mortality from amyotrophic lateral sclerosis in the US, 1991-1999. *Journal of exposure science & environmental epidemiology* 2015;25(1):65-71.

24. Koeman T, Slottje P, Schouten LJ, et al. Occupational exposure and amyotrophic lateral sclerosis in a prospective cohort. *Occup Environ Med* 2017;74(8):578-85.

25. Huss A, Spoerri A, Egger M, et al. Occupational exposure to magnetic fields and electric shocks and risk of ALS: the Swiss National Cohort. *Amyotroph Lateral Scler Frontotemporal Degener* 2015;16(1-2):80-5.

26. Chen GX, t Mannetje AM, Douwes J, et al. Occupation and motor neuron disease: a New Zealand case-control study. *Occup Environ Med* 2019;76(5):309-16.

27. Ministry of Health, New Zealand. National Minimum Dataset (hospital events). Wellington, New Zealand. https://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections/national-minimum-dataset-hospital-events. Published 1999. Updated July 1, 2017. Accessed September 18, 2019.

28. Alonso A, Logroscino G, Jick SS, et al. Incidence and lifetime risk of motor neuron disease in the United Kingdom: a population-based study. *European journal of neurology* 2009;16(6):745-51.

29. Stats New Zealand. New Zealand Standard Classification of Occupations 1999. Wellington, New Zealand. http://archive.stats.govt.nz/methods/classifications-and-standards/classification-related-stats-standards/download-the-classification-coding-system.aspx#gsc.tab=0. Published 2001. Updated August 3, 2015. Accessed September 18, 2019.

30. Stats New Zealand. Australian and New Zealand Standard Industrial Classification (New Zealand Use Version) 1996. Version 4.1. Wellington, New Zealand. http://archive.stats.govt.nz/methods/classifications-and-standards/classification-related-stats-standards/industrial-classification-1996.aspx#gsc.tab=0. Published 2002. Updated July 16, 2002. Accessed September 18, 2019.

31. Huss A, Vermeulen R, Bowman JD, et al. Electric shocks at work in Europe: development of a job exposure matrix. *Occupational & Environmental Medicine* 2013;70(4):261-7.

32. Koeman T, Slottje P, Kromhout H, et al. Occupational exposure to extremely low-frequency magnetic fields and cardiovascular disease mortality in a prospective cohort study. *Occup Environ Med* 2013;70(6):402-7.

33. Bowman JD, Touchstone JA, Yost MG. A population-based job exposure matrix for power-frequency magnetic fields. *Journal of occupational and environmental hygiene* 2007;4(9):715-28.

34. Department of Public Health. *NZDep2006 Index of Deprivation*. University of Otago, Wellington, New Zealand: Department of Public Health; 2007.

35. Jafari H, Couratier P, Camu W. Motor neuron disease after electric injury. *Journal of Neurology, Neurosurgery & Psychiatry* 2001;71(2):265-7.

36. Gawel M, Zaiwalla Z, Rose F. Antecedent events in motor neuron disease. J Neurol Neurosurg Psychiatry. *Journal of Neurology, Neurosurgery, and Psychiatry* 1983;46:1041-3.

37. Huynh W, Lam A, Vucic S, et al. Corticospinal tract dysfunction and development of amyotrophic lateral sclerosis following electrical injury. *Muscle Nerve* 2010;42(2):288-92.

38. Zoccolella S, Masi G, Mezzapesa D, et al. Motoneuron disease after electric injury: a case report. *Neurol Sci* 2008;29(1):47-9.

39. Vergara XP, Kheifets L, Silva M, et al. New electric-shock job exposure matrix. *Am J Ind Med* 2012;55(3):232-40.

40. Abhinav K, Al‑Chalabi A, Hortobagyi T, et al. Electrical injury and amyotrophic lateral sclerosis: a systematic review of the literature. *Journal of Neurology, Neurosurgery, and Psychiatry* 2007;78(5):450-3.

41. Andrews CJ, Reisner AD. Neurological and neuropsychological consequences of electrical and lightning shock: review and theories of causation. *Neural Regen Res* 2017;12(5):677-86.

42. Reisner AD. Possible mechanisms for delayed neurological damage in lightning and electrical injury. *Brain Inj* 2013;27(5):565-9.

43. Reisner AD. Delayed neural damage induced by lightning and electrical injury: neural death, vascular necrosis and demyelination? *Neural Regen Res* 2014;9(9):907-8.

44. Tsong TY, Su Z-D. Biological Effects of Electric Shock and Heat Denaturation and Oxidation of Molecules, Membranes, and Cellular Functions. *Annals of the New York Academy of Sciences* 1999;888(1):211-32.

45. Wang MD, Little J, Gomes J, et al. Identification of risk factors associated with onset and progression of amyotrophic lateral sclerosis using systematic review and meta-analysis. *Neurotoxicology* 2017;61:101-30.

46. Armstrong BG. Effect of measurement error on epidemiological studies of environmental and occupational exposures. *Occup Environ Med* 1998;55(10):651-6.

47. Turner MC, Benke G, Bowman JD, et al. Occupational Exposure to Extremely Low-Frequency Magnetic Fields and Brain Tumor Risks in the INTEROCC Study. *Cancer Epidemiology Biomarkers & Prevention* 2014;23(9):1863-72.

48. Huss A, Peters S, Vermeulen R. Occupational exposure to extremely low-frequency magnetic fields and the risk of ALS: A systematic review and meta-analysis. *Bioelectromagnetics* 2018;39(2):156-63.

19

49.   Savitz DA, Loomis DP, Tse CK. Electrical occupations and neurodegenerative disease: analysis of U.S. mortality data. *Archives of Environmental Health* 1998;53(1):71.

50.   Roosli M, Lortscher M, Egger M, et al. Mortality from neurodegenerative disease and exposure to extremely low-frequency magnetic fields: 31 years of observations on Swiss railway employees. *Neuroepidemiology* 2007;28(4):197-206.

51.   Pedersen C, Poulsen AH, Rod NH, et al. Occupational exposure to extremely low-frequency magnetic fields and risk for central nervous system disease: an update of a Danish cohort study among utility workers. *International Archives of Occupational and Environmental Health* 2017;90(7):619-28.

52.   Sorahan T, Mohammed N. Neurodegenerative disease and magnetic field exposure in UK electricity supply workers. *Occup Med (Lond)* 2014;64(6):454-60.

53.   Pearce N, Kromhout H. Neurodegenerative disease: the next occupational disease epidemic? *Occup Environ Med* 2014;71(9):594-5.

20

Table 1. Characteristics of Participants in a Population-Based Case-Control Study of Occupational Exposure to Electric Shocks and Extremely Low-Frequency Magnetic Fields and Motor Neurone Disease, New Zealand, 2013-2016

Characteristics	Male Cases (n=203)		Male Control (n=331)		p-Value[a]	Female Cases (n = 116)		Female Controls (n = 273)		P-Value[a]
	No.	%	No.	%		No.	%	No.	%	
Age at interview					0.0002					0.0466
20-49	20	9.85	16	4.83		10	8.62	24	8.79	
50-59	47	23.15	51	15.41		26	22.41	48	17.58	
60-69	79	38.92	112	33.84		44	37.93	76	27.84	
≥70	57	28.08	152	45.92		36	31.04	125	45.79	
Ethnicity					0.9462					0.1222
European/Pakeha[b]	188	92.61	304	91.84		106	91.38	259	94.87	
Māori[c]	8	3.94	14	4.23		5	4.31	11	4.03	
Pacific & others	7	3.45	13	3.93		5	4.31	3	1.10	
Deprivation Index Quintile					0.0237					0.1671
1-2 (least deprived)	76	37.44	83	25.08		23	19.83	82	30.04	
3-4	50	24.63	83	25.08		28	24.14	60	21.98	
5-6	32	15.76	71	21.45		35	30.17	58	21.24	
7-8	27	13.30	64	19.34		16	13.79	44	16.12	
9-10 (most deprived)	18	8.87	30	9.05		14	12.07	29	10.62	
Highest Education					0.4090					0.3952
Primary & secondary school	92	45.32	160	48.34		52	44.83	129	47.25	
Technical or trade school diploma	70	34.48	94	28.40		35	30.17	61	22.34	
Undergraduate university degree	27	13.30	45	13.60		18	15.52	53	19.41	
Postgraduate university degree	14	6.90	32	9.66		11	9.48	30	11.00	
Smoking (prior diagnosis)					0.6966					0.4711
Never	102	50.25	155	46.83		62	53.45	164	60.07	
Smoker at the time of diagnosis	16	7.88	25	7.55		4	3.45	9	3.30	
Ex	85	41.87	151	45.62		50	43.10	100	36.63	

[a] P-Values were calculated using a chi-square test for categorical variables.

[b] Pakeha (a Māori word) - this is used as a term specifically for New Zealand European people.

[c] Māori – indigenous people of New Zealand.

21

Table 2. Risk of Motor Neurone Disease with Occupational Exposure to Electric Shocks in a Population-Based Case-Control Study, New Zealand, 2013-2016

Exposure to Electric Shock	Cases (n=319)		Controls (n=604)		OR[a]	95%CI	OR[b]	95%CI
	No.	%	No.	%				
Background potential for shocks	143	45	338	56	1.00	Referent	1.00	Referent
Ever exposed above background level	176	55	266	44	1.39	1.04, 1.86	1.35	0.98, 1.86
Exposure level								
Background potential for shocks	143	45	338	56	1.00	Referent	1.00	Referent
Only medium potential for shocks	75	23	154	25	1.06	0.75, 1.50	1.07	0.74, 1.55
Ever high potential for shocks	101	32	112	19	1.99	1.37, 2.90	2.01	1.31, 3.09
Duration of exposure, years								
Background potential for shocks	143	45	338	56	1.00	Referent	1.00	Referent
Exposure <3 years	52	16	62	10	1.80	1.18, 2.75	1.85	1.18, 2.90
Exposure 3-8 years	36	11	72	12	1.05	0.66, 1.65	1.00	0.61, 1.62
Exposure 9-24 years	37	12	64	11	1.21	0.76, 1.94	1.12	0.67, 1.86
Exposure >24 years	51	16	68	11	1.52	0.97, 2.37	1.41	0.86, 2.28
P-value (test for trend)					0.69		0.45	
Background potential for shocks	143	45	338	56	1.00	Referent	1.00	Referent
Medium potential[c] <3 years	24	7	48	8	1.07	0.63, 1.84	1.12	0.64, 1.96
3-8 years	20	6	49	8	0.86	0.49, 1.52	0.85	0.47, 1.52
9-24 years	16	5	28	5	1.25	0.65, 2.40	1.21	0.62, 2.40
>24 years	15	5	29	5	1.22	0.62, 2.41	1.22	0.60, 2.47
Ever high potential[d] <3 years	28	9	14	2	4.42	2.20, 8.87	4.69	2.25, 9.77
3-8 years	16	5	23	4	1.59	0.89, 3.20	1.56	0.74, 3.29
9-24years	21	7	36	6	1.32	0.72, 2.43	1.27	0.65, 2.49
>24 years	36	11	39	6	1.95	1.14, 3.32	1.88	1.05, 3.36
Cumulative exposure, unit-years[e]								
Background potential for shocks	143	45	338	56	1.00	Referent	1.00	Referent
Exposure <4 unit-years	42	13	68	11	1.32	0.85, 2.04	1.34	0.85, 2.13
Exposure 4-16 unit-years	37	12	68	11	1.17	0.74, 1.86	1.17	0.72, 1.90
Exposure 17-52 unit-years	45	14	64	11	1.52	0.96, 2.39	1.45	0.88, 2.39
Exposure >52 unit-years	52	16	66	11	1.63	1.04, 2.56	1.53	0.92, 2.54
P-value (test for trend)					0.33		0.54	

Abbreviation: CI, confidence interval; ELF-MF, extremely low-frequency magnetic fields; OR, odds ratio.
[a] OR adjusted for age and sex.
[b] OR adjusted for age, sex, education, ethnicity, socioeconomic status, smoking status, sports, alcohol, head injury, spine injury, ELF-MF, and solvents.
[c] Duration above background (for those with medium exposure only).
[d] Duration above background (for those with ever high exposure).

[e] Cumulative exposure (unit-years) is the product of duration and level of exposure (background level assigned 0, medium level exposure assigned 1, high exposure level assigned 4).

Table 3. Risk of Motor Neurone Disease with Occupational Exposure to Electric Shocks with Different Lag Times in a Population-Based Case-Control Study, New Zealand, 2013-2016

Exposure to Electric shocks	Case		Controls		OR[a]	95%CI	OR[b]	95%CI
	No.	%	No.	%				
Lag time –Exposure above background								
5 years lag	(319)		(604)					
Background potential for shocks	143	45	340	56	1.00	Referent	1.00	Referent
Ever exposure above background level	176	55	264	44	1.41	1.05, 1.88	1.45	1.04, 2.02
10 years lag	(319)		(602)					
Background potential for shocks	145	45	344	57	1.00	Referent	1.00	Referent
Ever exposure above background level	174	55	258	43	1.44	1.08, 1.93	1.48	1.06, 2.05
20 years lag	(314)		(595)					
Background potential for shocks	147	47	351	59	1.00	Referent	1.00	Referent
Ever exposure above background level	167	53	244	41	1.50	1.12, 2.01	1.50	1.08, 2.09
40 years lag	(238)		(496)					
Background potential for shocks	126	53	314	63	1.00	Referent	1.00	Referent
Ever exposure above background level	112	47	182	37	1.40	1.00, 1.97	1.42	0.97, 2.08
Lag time –Medium and high level exposure								
5 years lag	(319)		(604)					
Background potential for shocks	143	45	340	56	1.00	Referent	1.00	Referent
Only medium potential for shocks	75	23	153	25	1.08	0.76, 1.53	1.14	0.79, 1.66
Ever high potential for shocks	101	32	111	19	2.02	1.39, 2.94	2.22	1.43, 3.43
10 years lag	(319)		(602)					
Background potential for shocks	145	45	344	57	1.00	Referent	1.00	Referent
Only medium potential for shocks	74	23	148	25	1.11	0.79, 1.57	1.17	0.81, 1.70
Ever high potential for shocks	100	32	110	18	2.04	1.40, 2.97	2.19	1.42, 3.39
20 years lag	(314)		(595)					
Background potential for shocks	147	47	351	59	1.00	Referent	1.00	Referent
Only medium potential for shocks	71	23	139	23	1.16	0.81, 1.65	1.19	0.81, 1.73
Ever high potential for shocks	96	30	105	18	2.09	1.43, 3.06	2.23	1.44, 3.46
40 years lag	(238)		(496)					
Background potential for shocks	126	53	314	63	1.00	Referent	1.00	Referent
Only medium potential for shocks	47	20	89	18	1.25	0.82, 1.90	1.25	0.80, 1.96
Ever high potential for shocks	65	27	93	19	1.58	1.03, 2.43	1.70	1.04, 2.79

Abbreviation: CI, confidence interval; ELF-MF, extremely low-frequency magnetic fields; OR, odds ratio.

[a] OR adjusted for age and sex.

[b] OR adjusted for age, sex, education, ethnicity, socioeconomic status, smoking status, sports, alcohol, head injury, spine injury, ELF-MF, and solvents.

23

Table 4. Risk of Motor Neurone Disease with Occupational Exposure to Extremely Low-Frequency Magnetic Fields in a Population-Based Case-Control Study, New Zealand, 2013-2016

Exposure to ELF-MF	Cases (n=319)		Controls (n=604)		OR[a]	95%CI	OR[b]	95%CI
	No	%	No.	%				
Background level	130	41	227	38	1.00	Referent	1.00	Referent
Ever exposed above background level	189	59	377	62	0.87	0.66, 1.15	0.77	0.56, 1.05
Exposure level								
Background level	130	41	227	38	1.00	Referent	1.00	Referent
Medium level only	161	50	326	54	0.87	0.65, 1.16	0.77	0.56, 1.06
Ever exposed at high level	28	9	51	8	0.88	0.52, 1.48	0.71	0.39, 1.28
Duration of exposure, years								
Background level	130	41	227	38	1.00	Referent	1.00	Referent
Exposure <3 years	55	17	99	16	0.95	0.64, 1.42	0.88	0.58, 1.35
Exposure 3-8 years	45	14	93	15	0.82	0.54, 1.25	0.74	0.47, 1.16
Exposure 9-23 years	40	13	92	15	0.78	0.50, 1.21	0.71	0.45, 1.13
Exposure >23 years	49	15	93	16	0.92	0.61, 1.40	0.73	0.46, 1.15
P-value (test for trend)					0.85		0.47	
Background level	130	41	227	38	1.00	Referent	1.00	Referent
Medium level[c] <3 years	40	12	77	13	0.91	0.58, 1.43	0.85	0.53, 1.35
3-8 years	41	13	79	13	0.89	0.57, 1.38	0.80	0.50, 1.28
9-23 years	37	12	86	14	0.79	0.50, 1.23	0.72	0.45, 1.16
>23 years	43	13	84	14	0.89	0.58, 1.38	0.71	0.45, 1.14
Ever high level[d] <3 years	15	5	22	4	1.07	0.53, 2.17	0.96	0.45, 2.07
3-8 years	4	1	14	2	0.46	0.15, 1.44	0.35	0.10, 1.21
9-23years	3	1	6	1	0.71	0.17, 2.95	0.50	0.11, 2.27
>23 years	6	2	9	1	1.22	0.41, 3.68	0.76	0.24, 2.41
Cumulative exposure, unit-years[e]								
Background level	130	41	227	38	1.00	Referent	1.00	Referent
Exposure <4 unit-years	52	16	96	16	0.93	0.62, 1.41	0.87	0.57, 1.34
Exposure 4-12 unit-years	47	15	106	17	0.77	0.51, 1.16	0.72	0.46, 1.11
Exposure 13-28 unit-years	43	13	83	14	0.93	0.60, 1.43	0.80	0.50, 1.26
Exposure >28 unit-years	47	15	92	15	0.87	0.57, 1.33	0.67	0.41, 1.07
P-value (test for trend)					0.96		0.42	

Abbreviation: CI, confidence interval; ELF-MF, extremely low-frequency magnetic fields; OR, odds ratio.

[a] OR adjusted for age and sex.

[b] OR adjusted for age, sex, education, ethnicity, socioeconomic status, smoking status, sports, alcohol, head injury, spine injury, electric shocks, and solvents.

[c] Duration above background (for those with medium exposure only).

[d] Duration above background (for those with ever high exposure).

[e] Cumulative exposure (unit-years) is the product of duration and level of exposure (background level assigned 0, medium level exposure assigned 1, high exposure level assigned 4).