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Mini Review

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A meta-analysis on residential exposure to magnetic fields and the risk of amyotrophic lateral sclerosis

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Abstract: Amyotrophic lateral sclerosis (ALS) is caused by the gradual degeneration and death of motor neurons, with mostly unknown etiology. Some risk factors have been suggested for this disease including extremely low frequency magnetic fields (ELF-MF) exposure. This meta-analysis assesses the association of residential exposure to ELF-MF with the risk of ALS. Five studies have addressed the risk of ALS in relation to overhead power lines. A pooled relative risk (RR) of 0.71 [95% confidence interval (CI): 0.48, 1.07] for the most exposed population group (either <200 m distance from high voltage power lines or >0.1 μT) was found. Little heterogeneity ($I^2 = 0.00\%$, $p = 0.67$) and indication for publication bias ($P_{\text{Begg's test}} = 0.22$; $P_{\text{Egger's test}} = 0.19$) was seen. Overall, we found no evidence for an association between residential exposure to ELF-MF and the risk of ALS, although the number of exposed cases is low.

Keywords: amyotrophic lateral sclerosis; magnetic fields; power line; residence.

Introduction

Amyotrophic lateral sclerosis (ALS) is a rare disease with an incidence of ~1.89 per 100,000-person years (1). Some unestablished environmental and occupational risk factors suggested for ALS are exposure to heavy metals, pesticides, solvents, electric shocks and extremely low frequency magnetic fields (ELF-MF) (2–4).

Long-term average residential exposure to ELF-MF is strongly affected by overhead high voltage power lines, distributed in rural and urban environments all over the world (5). Residential exposure to ELF-MF (6) is far lower than the reference level for general-public exposure at 50/60 Hz [200 μT (7)] but possible effects of MF on human health, especially onset of neurodegenerative diseases (NDD), have been suggested by some recent review studies (8, 9). Moreover, a few animal and in vitro studies that investigated NDD relevant end-points have shown that effects of exposure to ELF-MF are either lacking or indicating positive effects on neuronal viability and differentiation (10). The first study on residential exposures to ELF-MF and risk of NDD, conducted by Huss et al. in 2008, found a hazard ratio (HR) of 2.00 [95% confidence interval (CI): 1.21, 3.33] to die from Alzheimer's disease for people living at least 10 years within a 50-m distance from a high voltage power line. However, no significant ALS risk was found with any of the cases observed within the 50-m corridor of high voltage power lines (11). After that, additional studies were conducted in Brazil (12), Denmark (13), the Netherlands (14) and Italy (15).

In total, limited evidence and no meta-analysis are available on the relationship of residential exposure to ELF-MF and the risk of ALS. Moreover, as ALS is a rare disease and only a small proportion of the population lives close to overhead power lines, single studies have little statistical power. Therefore, this current meta-analysis aims to overcome this limitation and pool risk estimates from all epidemiological studies of residential ELF-MF exposure and the risk for ALS.

Methods

We considered all studies fulfilling the following inclusion criteria: (1) to have objective measures on residential exposure to ELF-MF, either distance or measured/modeled magnetic power flux density, (2) a risk estimate, such as odds ratio (OR), rate ratio or risk ratio for ALS or motor neuron disease (MND) – 90% of MND cases are ALS (16), (3) in the English language and peer-reviewed. In total, five studies fulfilling these criteria were identified (11–15) (Table 1).

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From each of these studies, we extracted the risk estimates for the highest exposed population group. We treated risk estimates of OR and HR as relative risk (RR) and standard errors (SEs) were calculated from the 95% CI.

The Q-test ($p<0.10$ as heterogeneity) and the I^2 statistics were used for the evaluation of heterogeneity. Given that no heterogeneity between studies was observed, a fixed-effect model was applied for pooled risk estimates. The funnel plot (data has not been shown), Begg's test and Egger's test for the assessment of publication bias were conducted. STATA 14 (Stata Corp, College Station, TX, USA) were used for all analyses.

Results

Table 1 indicated that from 2008 to 2017, four case-control studies and a cohort study were conducted, all in Europe, except for one from Brazil. The eligible studies used different sources for gathering outcome data but the International Classification of Disease (ICD) was applied as the outcome assessment method in all studies, except for the Seelen study (14).

An illustration of pooled risk estimate is presented in Figure 1. We found the pooled estimate of 0.71 (95% CI: 0.48, 1.07), resulted from the five studies. The results showed no heterogeneity ($I^2=0.00\%$, $p=0.67$) amongst the studies.

The funnel plot (Figure 2) shows no asymmetry (the plot is been shown), indicates no publication bias for the studies on the ALS risk and residential ELF-MF exposure. In addition, the results were confirmed by Begg's test ($p=0.22$) and Egger's test ($p=0.19$).

Table 1: Characteristics of studies on the association between residential exposure to ELF-MF and risk of ALS.

First author, year, (Ref.)	Country time period number of ALS/MND cases	Study design	Outcome: source of data assessment criteria	Exposure: source of residence data source of exposure assessment method creation	Covariates	Results: effect size value of effect size sex number of related cases
Huss, 2008, (11)	– Swiss – 2000–2005 – 744	Cohort	– DC[a] – ICD[c] – ALS[f]	– Census – 220–380 kV PLs[d] – DTPLs[g] – 50–200 m[h]	Sex, education, occupation, region, civil status, language, number of apartments per building and living within 50 m	– HR[b] – 0.85 (0.46, 1.59)[e] – Both – 10 exposed cases
Marcilio, 2011, (12)	– Brazil – 2001–2006 – 367	Case-control	– DC – ICD – ALS	– Death certificate – 88–440 kV PLs – DTPLs, Modeling of ELF-M[k] – <50 m	Sex, age, city of residency, race, schooling, marital status[l]	– OR[j] – 0.26 (0.06, 1.05) – Both – Two exposed cases
Frei, 2013, (13)	– Denmark – 1994–2010 – 2990	Case-control	– HDR[m] – ICD – MND[n]	– A population register-based database –132–400 kV PLs – DTPLs – <50	Income, education, urbanization category, number of floors in the residential building, marital status	– HR – 0.80 (0.34, 1.89) – Both – Seven exposed cases
Seelen, 2014, (14)	– The Netherlands – 2006–2013 – 1139	Case-control	– A prospective ALS study – Medical examination – ALS	– Municipal personal records database – 220–380 kV PLs – DTPLs – 50–200 m[h]	Sex, age	– OR – 0.73 (0.15, 3.50) – Both – Two exposed cases
Vinceti, 2017, (15)	– Italy – 1998–2011 – 703	Case-control	– HDR, DC, drug prescriptions records – ICD – ALS	– Revenue agency of the ministry of finance and the National health services directories – ≥132 kV – Modeling of ELF-MF – ≥0.1 μT	Sex, age	– OR – 0.65 (0.27, 1.55) – Both – Six exposed cases

[a]Death certificate; [b]hazard ratio; [c]International Classification of Disease; [d]power lines; [e]relative risk (95% confidence intervals); [f]amyotrophic lateral sclerosis; [g]distance of the place of residence to the nearest power lines; [h]no cases < 50 m; [j]odds ratio; [k]extremely low frequency magnetic fields; [l]ALS estimates not adjusted since only two cases occurred; [m]hospital discharge records; [n]motor neuron disease.

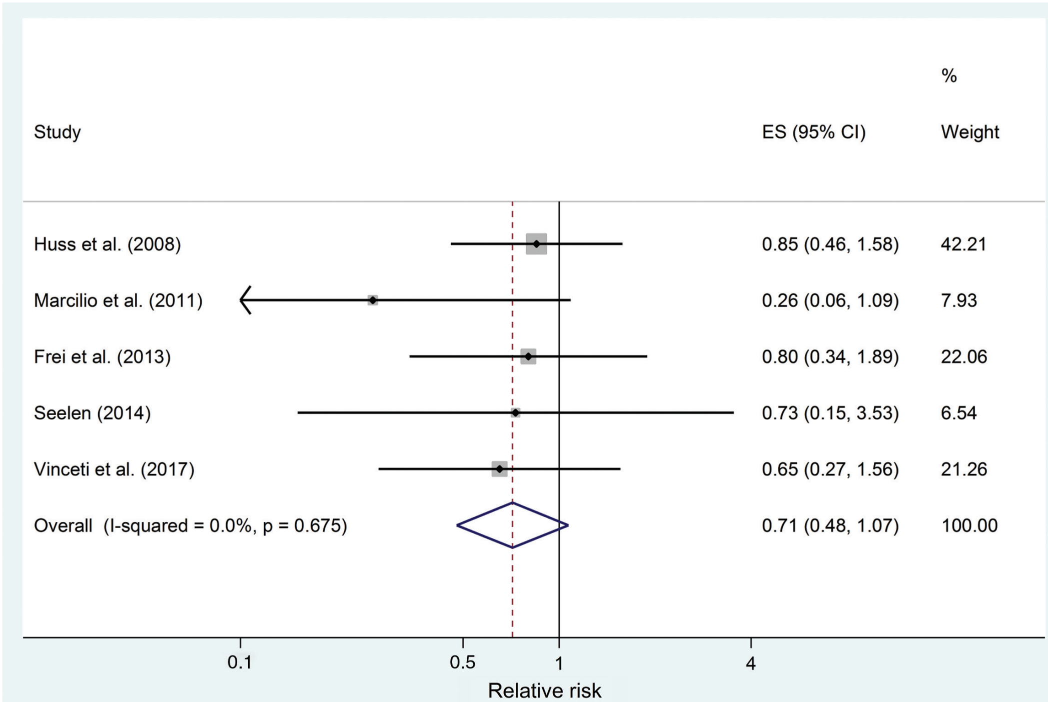

Figure 1: Forest plot of eligible studies on the ALS risk and residential exposure to ELF-MF.

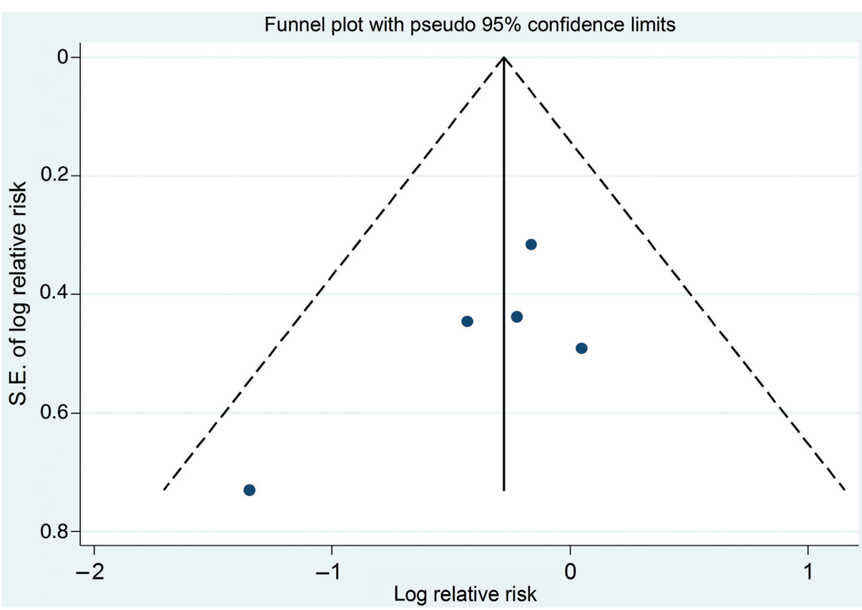

Figure 2: Funnel plot for all individual studies related to ELF-MF. Each point represents a separate study.

Discussion

To date, no meta-analysis has been conducted on the association of residential ELF-MF exposure with the risk of ALS. The current study does not provide indications for elevated ALS risk in relation to exposure from high voltage power lines. There was little heterogeneity and no evidence for publication bias. However, some limitations are seen in the studies.

Despite the pooling of all available studies, the number of exposed cases is small and thus some uncertainty persists. Most of the studies used the death certificate as the outcome data, which is inaccurate for many diseases. However, they are considered a reliable and valuable source for determining ALS in epidemiological studies, as ALS is fatal and occurs often at a relatively young age (17).

The definition of the exposed group was different among the studies. In two studies (11, 14) no cases were observed within 50 m of a highest voltage power line (>200 kV) and thus the risk estimates for a distance of 50–200 m were used. Two other studies (12, 13) also considered the distance to power lines <200 kV, where substantial MF exposure levels are rare (5). Only one study modeled MF but because only one cases occurred ≥0.4 μT related to an OR of 0.27 (95% CI: 0.04–2.13), we used the more robust estimate based on six cases exposed ≥0.1 μT. No study used direct the measurement method (usually called spot measurements) or the personal exposure method (usually called exposimetery), which is often considered the most accurate exposure assessment method (18). However, in this situation, where long-term exposure is most relevant, a simple proxy like distance may provide (19) unbiased estimates as it possibly avoids some of the biases introduced by more complex exposure measures (20). Most of the previous studies on ALS and MF considered occupational exposure (21–23). In some, but not all, of these studies occupational MF exposure was associated with ALS. This might indicate that only stronger MF, which sometimes occur in occupation settings, causes ALS. On the other hand, the occupational findings may be the consequences of publication bias or the inadequate control of confounding. For instance, electric shocks has been proposed as an alternative explanation for the observed increased ALS risk among electricians (19, 24).

Conclusion

In conclusion, based on the limited epidemiological research on this topic we found no association between residential exposure to ELF-MF and the risk of ALS.

Author Statement
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