

Neurodegenerative Diseases, Suicide and Depressive Symptoms in Relation to EMF

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In 1979 the first study was published which indicated that environmental exposure to power frequency, electric and magnetic fields (EMF), might increase the risk of chronic disease. This was a study on cancer. However, this research area has gradually evolved and come also to include outcomes other than cancer. The purpose of this paper is to provide a better understanding of the literature on neurodegenerative diseases and on suicide and depressive symptoms in relation to EMF by using a meta-analysis technique. It is concluded that for amyotrophic lateral sclerosis, there are relatively strong data indicating that electric utility work may be associated with an increased risk. However, EMF exposure is only one of several possible explanations to this. For Alzheimer's disease the combined data on an association with EMF are weaker than that for ALS. For suicide an overall assessment yields the conclusion that the support for an association is weak. For depressive symptoms the assessment is more complex, but the overall conclusion is nevertheless that the evidence is relatively weak. For other diseases, such as Parkinson's, there is not enough information for an assessment. Bioelectromagnetics Supplement 5:S132–S143, 2001. © 2001 Wiley-Liss, Inc.

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INTRODUCTION

In 1979 Wertheimer and Leeper presented the first study indicating that environmental exposure to power frequency (50 and 60 Hz), electric and magnetic fields (EMF) might increase the risk of chronic disease—in this case mortality—from cancer in children [Wertheimer and Leeper, 1979]. Three years later this study was followed by a report by Milham on the relation between cancer and work in occupations with presumed exposure to EMF [Milham, 1982]. These original studies have been followed by a substantial number of subsequent reports on various cancer diseases. To a certain extent these reports have confirmed the original findings, in particular with respect to childhood leukemia [NIEHS, 1998], and, although more weakly, with respect to brain cancer and leukemia in adults with occupational exposure. The established mode of interaction between EMF and humans is by means of induced currents, and sufficiently strong fields may result in acute health effects. Existing exposure guidelines provide restrictions on current densities that prevent effects on functioning of the nervous system. These limits, however, are orders of magnitude above those levels for which effects have been suggested in the cancer studies. In the case of environmental exposure, the fields are too weak to produce currents above the signal to noise ratio, and

consequently some other mechanism would be needed in order to explain an effect of EMF exposure. There is little support for the epidemiological findings that exposure to EMF might increase the risk of disease from in vitro and in vivo experimental research. Nevertheless, the epidemiological research has gradually expanded and has also come to include outcomes other than cancer. This review focuses on neurodegenerative diseases and on suicide and depression.

Hypotheses relating EMF to neurodegenerative diseases are a relatively novel part of the EMF research area and so far only a modest number of studies have been performed. However, this area has quickly acquired attention because it has been relatively easy to come up with suggestions for mechanisms [Sobel and Davanipour, 1996]. For a number of methodological reasons the neurodegenerative diseases are more difficult to study than, say, cancer. The most obvious difficulty is that neurological diseases are not recorded

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in registries in the same way as cancers and that mortality registries are less reliable as sources of cases. There are also difficulties related to factors such as lack of consensus on diagnostic criteria and difficulties in assessing time of disease onset. In addition, the gender difference in incidence rates, at least for Alzheimer's disease, makes it more difficult to base a study on occupational exposure, because women, who have the higher incidence, have less often been employed, particularly women currently in the age stratum where the incidence is high. These and other difficulties are reflected in the literature, and the studies that have best avoided these problems seem instead to suffer from small numbers. The overwhelming focus has been on two endpoints, namely Alzheimer's disease (AD) and amyotrophic lateral sclerosis (ALS), but there are some data also on Parkinson's disease.

Concerns about possible psychiatric or psychological effects of EMF exposure had been raised by investigators from the Soviet Union in the late 1960s and early 1970s, based on anecdotal reports of symptoms such as insomnia, memory loss, and headache [Asanova and Rakov, 1972]. However, these and other early reports have basically remained unconfirmed [Knave et al., 1979]. In the late 1970s the first study was published that suggested a link between EMF and suicide [Reichmanis et al., 1979]. This has now been followed up by other studies on suicide and also on depressive symptoms. An inspiration for this research may have been that it has been relatively easy to formulate biologically plausible hypotheses, based on EMF effects on the circadian rhythm or melatonin synthesis, that might explain a potential link between EMF and depression [Wilson, 1988].

The purpose of this paper is to provide a better understanding of this literature by using a meta-analysis technique. This implies conducting a review of the literature that rests as much as possible on a systematic and quantitative analysis. However, given the relatively small number of available studies for each of the various endpoints, there is an obvious limitation to what the quantitative approach can achieve.

MATERIAL

The material in a meta-analysis, as in all other reviews, consists of the scientific studies on the topic in question. The studies for this review were identified according to the following procedure: The starting point was the material used at the EMF science review symposium that was organized in January, 1998, by the US National Institute of Environmental Health

Sciences as part of the EMF RAPID program [NIEHS, 1998]. This material was collected through an extensive literature search. In order to update this material with studies that may have become available after January, 1998, a group of scientists with documented knowledge of this research area was asked whether they were aware of any new studies that had become available after the NIEHS symposium. A new computerized literature search was also done. No new studies were identified through this process, but some studies that were only available in manuscript in January, 1998, were now identified as published.

For a study to be eligible for this analysis, it had to analyze the risk, of some of the diseases in question in a population with elevated EMF exposure in relation to a reference population. The study had to report a quantitative relative risk estimate with a confidence interval or data that permitted the calculation of those. Only papers published in the scientific literature were defined as eligible. However, we were not aware of any studies available only in manuscript or some other form of non-published report.

METHODS

All the identified reports were studied and information of relevance for the interpretation was noted. This information was divided into the following areas. First, aspects of importance for the evaluation of susceptibility to selection bias were extracted. These included the relation between the study population and the mechanisms by which cases and controls, as well as response rates or participation rates, were identified. Included here also are issues related to the diagnoses and diagnostic criteria. Second, the definitions of EMF exposure and sources of information for exposure assessment were reviewed and noted. This included whether job titles were used as the basis for exposure definition, whether these were linked to measurements or not, where the job title information was obtained, etc. Third, the magnitudes of the observed effects and confidence intervals were recorded; the width of the confidence interval summarizes the effective size of the study. In those instances where more than one effect estimate was reported, an attempt was made to choose the one most specifically related to EMF exposure and the one related to the highest level of exposure. In many of the reports this choice is of little consequence for the result, but in some studies the result depends considerably on how EMF exposure is specified. These situations are noted in the text and the differences are discussed. Finally, an overall assessment of the study was made, including an assessment

of the most critical aspect for the evaluation of the study.

Pooling, that is estimation of the average effect across studies, was done with a fixed effects model using weights proportional to the inverse of the variance estimates from the individual studies [Fleiss, 1993]. Homogeneity testing was also performed, but did not result in any statistically significant results. Pooling was done across all identified studies in a diagnostic group and after stratification or restriction by certain study characteristics. An attempt was made to identify subgroups of more reliable and valid studies and to pool across the studies in such groups.

RESULTS

Amyotrophic Lateral Sclerosis (ALS)

Seven studies on ALS were identified that fulfilled the eligibility criteria for this analysis [Deapon and Hendersen, 1986; Gunnarsson et al., 1991; Gunnarsson et al., 1992; Davanipour et al., 1997; Johansen and Olsen, 1998; Savitz et al., 1998a,b]. Certain characteristics of these studies are displayed in Table 1. All the studies are based on occupational exposure to EMF. Some used job title on the death certificate or in a census as a proxy for exposure; others used job history accompanied with a job exposure matrix or some other

TABLE 1. Certain Characteristics and Findings of Studies on the Relation Between EMF and ALS

Reference	Study population and subject identification	Definition and estimation of exposure	Study design	Numbers	Result RR (95% C.I.)
Deapon and Hendersen [1986]	Study population: not specified Cases: ALS society, USA in 1979 Controls: friends	Questionnaire: electrical occup 3 years prior to diagnosis	CC	518 cases (19 electr. occ.) 518 controls (5 electr. occ.)	3.8 1.4–13.0
Gunnarsson et al. [1991]	Male population of Sweden 1970–1983 Cases: deaths with ALS as underlying or contributing cause in mortality registry Controls: random sample from population	Job title in census 1960: electricity worker	CC	1067 cases (32 exposed) 1005 controls	1.5 0.9–2.6
Gunnarsson et al. [1992]	Male population of central and southern Sweden in 1990 Cases: patients with MND in neurological departments Controls: random sample from population	Questionnaire: electricity work and exposure to MF	CC	58 cases (4 MF exposure) 189 controls	0.6 (MF exp) 0.2–2.0
Davanipour et al. [1997]	Study base: not specified Cases: ALS patients at outpatient clinic in southern California Controls: relatives	Questionnaire about occupational history: EMF exposure assessed by hygienist. Cumulative (E1) and average (E2) exposure	CC	28 cases 32 controls cut off: 75th percentile, of case distribution	2.3 0.8–6.6 average (E2)
Savitz et al. [1998a]	Male population in 25 states, US, 1985–1991 Cases: deaths from ALS Controls: deaths from other causes	Job title on death cert.: electrical occupation in aggregate and individual jobs	CC	114 cases in electr. occup. in aggregate	1.3 1.1–1.6
Savitz et al. [1998b]	Male employees at five US utility companies 1950–1988 Cases: deaths with ALS mentioned on death certificate, identified through multiple tracking sources	Measurements and employ- ment records. Combi- nation of duration and EMF index	Cohort	9 cases with >20 years in exposed occup.	2.4 0.8–6.7
Johansen and Olsen [1998]	Male employees in Danish utility companies observed during 1974–1993 Cases: deaths from ALS in mortality registry	Employment records and JEM: estimated average exposure level	Cohort	21236 males in cohort 9 exposed cases	2.5 1.1–4.8

TABLE 2. Pooling Across Groups of Studies on EMF and ALS

Pooled studies	Number of studies	RR	95% C.I.
All	7	1.5	1.2–1.7
Clinically and ALS society based studies	3	3.3	1.7–6.7
Mortality registry and census based studies	2	1.3	1.1–1.6
Utility cohorts studies	2	2.7	1.4–5.0

exposure index to assess EMF exposure. The methods for diagnosis and case ascertainment varied across studies. Some used death certificate information, while others used cases from specialized neurological clinics. All the studies provided some degree of support for a relation between EMF exposure and ALS risk, although the strength of the support varied considerably because of study characteristics. It is clear that there are considerable differences in the design of these studies in terms of overall study characteristics and specifically in terms of methods for the identification of study subjects, as well as in the definition and assessment of EMF exposure. Even though the differences in results between these studies are not strikingly large, it is clear that because of the design differences there is a weak basis for assuming homogeneity. With that in mind, the first line of Table 2 does provide the pooled result across all those seven studies as a crude way of summarizing the literature. The overall relative risk is estimated at 1.5 (95% CI = 1.2–1.7).

The seven studies may be divided into three groups according to design features. One group consists of the three studies that did not use mortality registries to recruit the cases, but instead identified them from neurological clinics or in one instance from an ALS society. Two of those are clinically based and lack specified population bases from which the cases are generated, and they use friends and relatives as the sources for controls [Deapen and Hendersen, 1986; Davanipour et al., 1997]. Thus, these two studies are susceptible to selection bias, the direction or magnitude of which can not be predicted with any certainty. Therefore, despite other assets, such as specific diagnoses and careful exposure assessment in one of them, the weight given to them in the overall assessment will be light. The third study in this group has a clearly defined study population from which in principle all prevalent and diagnosed cases are identified and the controls constitute a random sample from that population [Gunnarsson et al., 1992]. Exposure assessment in this study, however, was based on a questionnaire with rather crude questions regarding electricity work and occupational exposure to EMF. It is not quite clear how these questions were asked but they appear to be of the type, “Have you ever experienced . . . ?”.

Analyses related to two questionnaire questions of relevance to this review are reported in the paper. These two questions, electricity work and EMF exposure, however, gave contradictory results. Electricity work was associated with an excess risk but EMF exposure was not so associated; the reasons for this are not explored in the paper. Hence, this study will also be given a relatively light weight in the overall assessment. The second line of Table 2 gives the pooled result across the three studies in this group, estimated at 3.3 (1.7–6.7).

The next group consists of two studies that are both based on death certificates for the identification of cases and on job titles for the assessment of exposure, in one case from death certificates and in the other from a census. The strengths of these two studies include the small risks of selection or recall bias that are consequences of the reliance upon registry information. Also the large numbers of subjects, as reflected by the narrow confidence intervals, are considerable assets. The major weakness is the crude information on which exposure assessment is based. It is based only on job title without any measurement or other data to back it up. In addition, work history is not considered, but only job title at one point in time. The pooled result of the studies in this group are given in Table 2 on line three. The overall relative risk is estimated at 1.3 (1.1–1.6).

The third group, finally, is made up of the two latest studies that are based on cohorts of utility workers, one in Denmark and one in the US [Johansen and Olsen, 1998; Savitz et al., 1998a]. Both these studies are designed such that the risk of selection bias is small, since they start with a well defined cohort and since deaths are searched for in mortality registries. Both studies also have employed detailed procedures for exposure assessment that involved classification of jobs based on measurements and also duration of jobs. Despite the large nominal sizes of the cohorts, however, the effective numbers of exposed cases are modest. These two studies are by far the ones that carry most of the weight in the overall analysis. The designs of the two studies are relatively similar and so are the findings. The combined results from these two studies are given on the last line of Table 2. The combined relative risk estimate is 2.7 (1.4–5.0).

In summary, the studies that have the highest propensity to selection bias also have the highest combined relative risk and the studies with the crudest exposure assessment have the lowest combined relative risk. The two studies with the most valid designs and most thorough exposure assessments provide a pooled relative risk in between the other two.

An additional study had an overall design similar to those in the second group of studies discussed above and was based on virtually the same data as the Savitz et al. [1998b] study. Death certificates provided information both on causes of deaths and job titles [Schulte et al., 1996]. However, this study did not focus on EMF and did not report the findings in such a way that a pooling was considered meaningful. The study looked at PMR-values for different job titles, but rather than defining and analyzing job titles linked to EMF exposure, it ranked the job titles according to risk. Although several occupations with presumed EMF exposure ranked high in this study, it is not possible to estimate the ALS risk for EMF exposed workers because job titles are only mentioned if they rank high, but not otherwise. Yet, another study has looked at ALS mortality by occupational group, but without being included in the above analyses [Strickland et al., 1996]. This study does not specifically report mortality in electrical occupations or in other occupations selected for their likelihood to entail EMF exposure. This study does, however, show some excess risk for welders but based on very small numbers.

Alzheimer's Disease

Five studies on AD fulfilled the criteria for the meta-analysis [Sobel et al., 1995, 1996; Feychting et al., 1998; Savitz et al. 1998a,b]. (see Table 3). These studies vary considerably with respect to design characteristics, and just as for the studies on ALS there is no justification for assuming homogeneity across the studies. Nevertheless the pooled result across all five studies is given in Table 4 on the top line, again to provide a very crude summary of the results. The combined relative risk is 2.2 (1.5–3.2).

The first two studies were clinically based case-control studies. The first combined three series of AD patients, one from the US and two from Finland [Sobel et al., 1995]. These series come from neurological centers that are specialized in diagnoses and treatment of AD and can therefore be assumed to be based on high quality diagnoses. One of the series used vascular dementia patients as controls; the second, other patients without neurological disease; and the third, neighborhood controls. The second study emanates partly from the same group of investigators and was an attempt to confirm the findings from the first [Sobel

et al., 1996]. It was also based on patients from a specialized clinic in the US and used another group of patients as controls. Both studies base exposure classification on occupational histories: Primary occupations are grouped into high, medium, and low exposure based on measurements. Both these studies share the same strengths and weaknesses. The strengths are high diagnostic specificity, good exposure classification, and relatively large study sizes. The major weakness is the lack of a specified study population and thus the potential for selection bias. The authors argue that such a bias is most likely to result in an attenuation of risk because the high diagnostic specificity in the case group may have resulted in the inclusion of AD patients among the controls. This may well be correct, but the unspecified way through which the subjects are selected opens the way for other potential problems and it remains impossible to assess direction or magnitude of a possible bias. These two studies are relatively similar in design. The pooled relative risk estimate across the two studies is 3.2 (1.5–5.4) as reported in Table 4.

Of the three remaining AD studies, one was based on the Swedish Twin Registry; and a follow up of the twins that was set up for the purposes of genetical studies of dementia in twins [Feychting et al., 1998]. Exposure to EMF was assessed through interviews that included job history. Jobs were classified according to EMF exposure based on measurements performed in connection with an earlier study on occupational EMF exposure and cancer [Floderus et al., 1996]. Both primary occupation and last occupation were used. Diagnostic quality in the study was good, as was EMF exposure assessment, and the population basis for the study was also good. The main problem with this study was its small size, as reflected by the relatively wide confidence intervals. It also has a contradiction in its findings. The two previous studies looked at *primary* job for defining occupational EMF exposure [Sobel et al., 1995, 1996]. When this was applied to the Twin Registry study, no excess risk was found. However, when the *last* occupation was used for the twins, a considerable excess risk was noted. It is not clear how one can explain why such differences in results depend on how the occupation is selected for which EMF exposure is assessed. Whether or not to conclude that this study replicates the finding in the previous two studies depends on the resolution of this inconsistency.

The last two studies to be included here were already discussed in the ALS section above, because they had provided data on both diseases. These are the US death certificate study and the US utility worker study [Savitz et al., 1998a,b]. As already discussed in

TABLE 3. Certain Characteristics and Findings of Studies on the Relation Between EMF and AD

Reference	Study population and subject identification	Definition and estimation of exposure	Study design	Numbers	Result RR (95% C.I.)
Sobel et al. [1995]	Study population: not specified Cases: three series of AD patients examined, 77–93, at one neurological clinic in the US and two in Finland Controls: three series—(1) vascular dementia patients, (2) patients without neurological disease, (3) neighborhood controls	Interview data on primary occupation. Classification into high/medium vs. low EMF exposure	CC	386 cases (36 exposed) 475 controls (16 exposed)	3.0 1.6–5.4
Sobel et al. [1996]	Study population not specified Cases: patients with probable or definite AD treated at AD medical center in California, US Controls: patients who were cognitively impaired or demented	Statewide data form information on primary occupation. Classification into high/medium vs. low EMF exposure	CC	326 cases 152 controls	3.9 1.5–10.6
Feychting et al. [1998]	Study population: subsample of the Swedish Twin Registry Cases: Identified through a screening and evaluation procedure Controls: intact twins with one twin in each of two control groups when two twins were eligible	Interviews. Primary and last occupation. Classification into three levels, based on JEM, highest >0.2 μ T	CC	55 cases 228 and 238 controls Similar with other control group	0.9 (primary) 0.3–2.8
Savitz et al. [1998a]	Male population in 25 states, US, 1985–1991 Cases: deaths from AD Controls: deaths from other causes	Job title on death cert.: electrical occupation in aggregate and individual jobs	CC	256 cases in electr. occup. in aggregate	1.2 1.0–1.4
Savitz et al. [1998b]	Male employees at five US utility companies 1950–1988 Cases: deaths with AD mentioned on death certificate identified from multiple tracking sources	Measurements and employment records. Combination of duration and EMF index	Cohort	16 cases with >20 years in exposed occup.	1.4 0.7–3.1

the ALS section, both of these are reliable studies; but the death certificate study has crude occupational data to base the EMF exposure assessment upon. The utility worker study has a sound design for AD just as well as for ALS. However, the study reports results both for underlying cause of mortality and for mentioned cause, and there is a difference between those results. When mentioned cause is used, there is little support for an association between EMF and AD, while the use of underlying cause gives some support for such an association. Because of the nature of this disease it seems more logic to look at mentioned cause, and this is the one used in this review whenever there has been a choice. However, one should keep in mind that there is no guarantee that the classification scheme is applied consistently when the death certificates are written.

The results of these three later studies are given individually in Table 3. For the combined studies, the relative risk is given on the bottom line of Table 4. The relative risk is 1.2 (0.7–2.3).

Two additional studies provide information without fulfilling the criteria to be considered for pooling. One is the study that was described in the ALS section, which used ranking of job titles as a means to report the findings [Schulte et al., 1996]. This study gave little indication that occupations with presumed exposure to EMF were linked to higher risk of AD. Second, the Danish utility worker study, which was discussed in relation to ALS, looked at all mortality, including dementia [Johansen and Olsen, 1998]. However, the diagnostic categories that were used did not specify AD, but only senile dementia and presenile dementia.

TABLE 4. Pooling Across Groups of Studies on EMF and AD

Pooled studies	Number of studies	RR	95% C.I.
All	5	2.2	1.5–3.2
Clinical based studies	2	3.2	1.9–5.4
Population based studies	3	1.2	0.7–2.3

Only one case of senile dementia and no case of presenile dementia were observed in the high exposure category. It is thus clear that even with a diagnostic classification that would specify AD, these data would not provide any support for an association between EMF and AD. On the other hand, numbers are so small that it does not provide evidence to the contrary, either.

Suicide and Depression

The studies on EMF and suicide are summarized in Table 5. The first of these was published as early as 1979 and has been followed by four more studies, the latest published in 1998. The first study, done in England and based on 589 suicide cases and controls, was done in two steps. In the first step, EMF was estimated based on nearby power lines; and in the second, measurements were taken in the homes of the study subjects [Reichmanis et al., 1979; Perry et al., 1981]. The study did find higher fields at case homes than in control homes. However, the study is methodologically limited and has been criticized both for the ways that subjects were selected and for the statistical analyses. The subsequent studies were high quality studies, and none of them provided support for the findings in the original study. The first two of these had relatively crude designs, particularly with respect to exposure assessments, in that one used distance to transmission facility and the other job title on death certificate [McDowall, 1986; Baris and Armstrong, 1990]. The latest two were based on cohorts of utility workers that were set up specifically for the purpose of studies on EMF, and they used thorough exposure assessments and follow up procedures [Baris et al., 1996a,b; Johansen and Olsen, 1998]. Because of the considerable design differences between these studies, it was not considered meaningful to undertake any pooling across studies.

The next set of studies address depression more directly (Table 6). The first two of them are difficult to interpret because of methodological limitations related to the procedures for selection of study subjects and also because they did not use validated scales for identification of depressive symptoms [Dowson and Lewith, 1988; Perry et al., 1989]. In addition, the study by Perry et al. also reports high average EMF levels

that remain unexplained—2.3 and 2.1 mG (0.23 and 0.21 μ T), respectively.

The remaining studies all used validated depression scales. One of these studies showed a clear association between proximity to power line and depression [Poole et al., 1993], while the other three provided little evidence for such an association [McMahan et al., 1994; Savitz et al., 1994; Verkasalo et al., 1997]. The study by Poole et al. is well designed and compares subjects on properties abutting a power line right of way to subjects further away, and the results appear internally consistent. They report a relative risk of 2.8 (95% CI = 1.6–5.1). The McMahan et al. study has a rather similar design and measurements to show that the homes close to the line have considerably higher EMF levels than homes further away. This study also appears valid but yields a relative risk of 0.9 (95% CI = 0.5–1.9). McMahan offers a number of possible explanations to the lack of consistency between these two studies, but none of those appears as the obvious answer.

The study by Savitz et al. is based on occupational exposure and shows no association for electrical workers in aggregate, although there are some indications for specific jobs. Finally, the Finnish twin registry study combines a depression scale applied to the Twin Registry with data on residential magnetic fields. Overall there is no relation between estimated EMF and the Beck Depression Inventory score that they used. There is, however, a clear excess risk for severe depression among those living within 100 meters from transmission lines. Just as for depression, pooling across studies was not considered meaningful.

Other Neurodegenerative Diseases

The only other neurodegenerative diseases to be mentioned in this context are Parkinson's disease and multiple sclerosis. However, data on their relation to EMF and other environmental factors are very sparse. Both the Danish and the US utility worker cohorts provide figures on Parkinson's disease, but the small numbers preclude any conclusions. The same is basically true for a study by Wechsler et al. [1991] that looked into a number of occupational factors in relation to Parkinson's disease. It did indicate an associ-

TABLE 5. Certain Characteristics and Findings of Studies on the Relation Between EMF and Suicide

Reference	Study base and subject identification	Definition and estimation of exposure	Study design	Numbers	Result RR (95% C.I.)
Reichmanis et al. [1979] and Perry et al. [1981]	Suicide victims and controls in England	Estimates of residential exposure from power lines. Measurements at the homes of subjects	CC	589 suicide cases	Higher estimated and measured fields at case homes
McDowall [1986]	Persons resident in the vicinity of transmission facilities, in specified areas in the UK, at the time of 1971 Census	Home within 50 m from substation or 30 m from overhead line	SMR	8 cases	0.75 (non-significant)
Baris and Armstrong, [1990]	Deaths in England and Wales during 1970–1972 and 1979–1983	Job titles on death certificates. Electrical workers in aggregate as well as specific jobs	PMR	495 suicide cases in electrical occupations	No increase for electrical workers
Baris et al. [1996 a,b]	Male utility workers, Quebec, Canada 1970–1988 Cases: deaths from suicide in mortality registry Controls: 1% random sample from the cohort	Job exposure matrix based on positron measurements was created. E-and B- and pulsed fields from average and geometric means and from cumulative and current exposure	CC	49 cases of suicide 215 controls	No evidence for magnetic fields. Some support for some electric field indices
Johansen and Olsen [1998]	Male employees in Danish utility companies observed during 1974–1993 Cases: deaths from suicide in mortality registry	Employment records and JEM: estimated average exposure level. Medium and high exposure	SMR	21236 males in cohort exposed cases	1.4 (non-significant)

ation with welding, though. In a separate paper published after the EPRI workshop, the Danish utility cohort was also used to look at MS in relation to EMF [Johansen et al., 1999]. No effect was seen but again, data were sparse.

DISCUSSION

Amyotrophic Lateral Sclerosis

The combined result from the two utility worker studies shows a clear increase in ALS mortality, and based on the combined confidence interval this risk-increase is unlikely to be due to chance. There is no obvious bias in design, such as exposure or diagnosis misclassification, that could explain the elevated risk. If anything, such a bias would have resulted in an attenuation of the relative risk. The two utility worker studies combined provide relatively strong evidence that work with EMF exposure in the utility industry is indeed related to increased ALS mortality. This result is reinforced by the other studies on ALS that are discussed above, even though those studies have to be given less weight.

Yet, one would like confirmatory results from even more studies, in particular studies specifically designed for the purpose. Assuming that the observed risk elevation is accurate, it still remains to be explained. Aside from the hypothesis that EMF exposure increases ALS risk, one must consider alternative explanations. One such alternative would be confounding from electric shock exposure. It is not inconceivable that exposure to electric shocks increases ALS risk and also that work in the utility industry carries a risk of experiencing electric shocks. As far as significant shocks are concerned this alternative explanation could be tested through confounding control in the usual way, assuming that information regarding the shocks could be obtained. It is more difficult to develop a method to test the importance of less significant shocks, which may not be recorded or result in medical treatment. Some of the reviewed studies did report analyses that indeed linked electric shocks to ALS [Deapen and Hendersen, 1986; Gunnarsson et al., 1992; Johansen and Olsen, 1998], but none of the studies provided an analysis in which the relation between EMF and ALS was studied with control for electric shocks. A crude calculation can be made from

TABLE 6. Certain Characteristics and Findings of Studies on the Relation Between EMF and Depression

Reference	Study base and subject identification	Definition and estimation of exposure	Study design	Numbers	Result RR (95% C.I.)
Dowson et al. [1988]	Persons in England who lived near 132 kV line and persons who lived 3 miles away. Questionnaire asking about depression	Distance between home and overhead line	Cross-sectional	132 near line, 9 with depression and 94 away from line, 1 with depression	Strong association depression, proximity to overhead line
Perry et al. [1989]	Persons discharged with depression from hospital, England and controls from electoral list	Measurements at front doors. Average for case and control groups compared	CC	359 patients discharged with diagnosis depressive illness	Average measurement in cases 2.3 mG and in controls 2.1 mG
Poole et al. [1993]	Residents in eight towns along a transmission line right-of-way in the US, 1987. A sample was interviewed. Depressive symptoms were obtained by Center for Epidemiologic Studies-Depression scale. Cut off for depression was median of score	Distance from power line: near vs. far. Near: properties abutting r-o-w or towers visible	Cross-sectional	382 persons interviewed	2.8 1.6–5.1
Savitz et al. [1994]	Male veterans who served in the US army first time 1965–1971. Two diagnostic inventories were used: the Diagnostic Interview Schedule and the Minnesota Personality Inventory. Life time depression used for report here	Present job identified in interview together with duration. Electrical worker	Cross-sectional	183 electrical workers (13 with life time depression) 3861 non-electrical workers	1.0 0.5–1.7
McMahan et al. [1994]	Population of neighborhood near a transmission line in Orange County, CA, USA, 1992. A sample of homes near a power line and one block away from the power line. Depressive symptoms identified through questionnaire and CES-D scale	EMDEX measurements at the front door. Average for homes on easement: 4.86 mG and one block away: 0.68 mG	Cross-sectional	Total of 152 women	0.9 0.5–1.9
Verkasalo et al. [1997]	Finnish twins who had answered the Beck Depression Inventory in 1990	Residential magnetic field estimated from power lines near the homes	Cross-sectional	12063 persons	BDI scores not related to exposure

data provided by Deapen and Hendersen, and this seems to indicate that the EMF association holds up even after control for electric shock experience.

Thus, the data provide relatively strong evidence for an increased risk of ALS in electrical utility work. EMF exposure, however, is only one of several possible explanations.

Alzheimer's Disease

Evaluated across all the studies, there appears to be a considerable association between estimated EMF exposure and AD risk. However, this result is mainly confined to the first two US studies, and it is not clearly confirmed by the later studies, with a possible exce-

ption for the Swedish Twin Registry study. All the studies have their strengths and weaknesses. The two original studies that show excess risks have the problem that they may be affected by some sort of selection bias, but one that is difficult to evaluate in terms of both magnitude and direction. Since the study populations are undefined, there is no way of determining to what extent the controls are representative with respect to exposure of the population from which the cases have emanated. As has been discussed in a previous section the US utility worker study has a valid design and there is no clear confirmation from this study of a link between EMF and AD. However, there is one problem in that the results to some extent depend on whether AD is mentioned cause or underlying cause as it is used in the analysis. Because of the internal inconsistencies in the results of the Swedish twin study it is somewhat difficult to assess whether this study supports the original findings or not. Overall, however, the support for the hypothesis of an association between EMF exposure and Alzheimer's Disease is mainly driven by findings from two clinically based case-control studies that must be interpreted with caution. Later studies have mainly failed to confirm this original.

Thus, taken together, the support for the hypothesis that occupational EMF exposure increases the risk for AD is considerably weaker than for ALS.

Suicide and Depression

When assessing the overall literature on EMF and suicide, it is necessary to consider the relative weight of the available studies together with their result. In doing so the original study must be given a relatively light weight in relation to the later studies because of methodological limitations. This is the only study that suggests a relation between EMF and suicide. The other studies provide little support for this hypothesis.

The overall conclusion is that there is weak support for the hypothesis that EMF exposure increases the risk of suicide.

The literature on depressive symptoms and EMF is somewhat difficult to interpret in that the findings are not consistent. This complexity cannot easily be resolved by suggesting that one type of results is confined to a group of studies with methodological problems or some other limitation. One could argue that the two studies by Dowson et al. and Perry et al. should be given lesser weight for methodological reasons, but not the study by Poole. In addition, there are certain indications in the remaining studies of a relation between EMF and depressive symptoms, although the main findings in these certainly are negative.

Overall, with three valid studies being mainly negative and only one clearly positive, the support for the hypothesis of a relation between EMF and depressive symptoms is rather weak.

Other Neurodegenerative Diseases

Only for Parkinson's disease and multiple sclerosis are some data available. However, small numbers preclude any conclusions.

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APPENDIX: DISCUSSION AT WORKSHOP

Bowman disagreed with the suggestion that shock could be explaining the association. The only study that had direct data of subjects experiencing shock was the study by Deven and Henderson that had the selection bias problems. Controlling for shock depresses the odds ratios a little; clearly shock does not explain the association with electrical work.

He also pointed out that both utility workers studies used job exposure matrices to get magnetic field exposures. So the association is not just with electrical work, it is with magnetic field exposure. Bowman agrees that the evidence of an association is moderate, but he feels that it is certainly far above the evidence for suicide and depression. The only firm diagnosis of Alzheimer's disease is based on autopsy. So the clinically based studies had, for the most part, diagnoses that were confirmed by autopsy, while the population-based studies were in some cases based on very ambiguous death certificates. In the Swedish twin study there was a clinical diagnosis, but it had not been confirmed by autopsy yet. In both ALS and Alzheimer's genetic factors have only been controlled in the clinically based studies, where they could ask about family history of neurodegenerative diseases. That is a strong modifying factor that resulted in a stronger association. For those reasons he put more weight on the clinically based studies that did find significant association. Others disagreed with the belief that genetic factors could be a strong confounder, because for both Alzheimer's and ALS genetics affect considerably less than 5% of all cases. Ahlbom replied that he would rank ALS as the most credible association. Alzheimer's would be the second, depression would be the third, and suicide would be the fourth.

Savitz wondered whether the melatonin idea and its link to depression is compelling enough to make a case for further research. Ahlbom thought that the extent to which EMFs affect melatonin in humans is still unclear. He further noted that suicide is in most of the cases, mostly a manifestation of depression so one could also think of combining these studies into one group, and then the overall association would become weaker again. Carpenter thought it very unlikely that melatonin could explain depression because the depression that one gets with long winter days is concomitant with a decreased excretion of melatonin, not an increase. He recalled that the New York state power-lines project produced evidence from chronic exposures to monkeys of a dose-dependent alteration in the

metabolism of the neurotransmitter dopamine. The major neurochemical change in patients with depression is a reduction of brain dopamine. Almost every drug used to treat most mental illness, but specifically depression, are dopamine antagonists. He thought that because of this measurable biomarker, even a tenuous epidemiological evidence should be pursued.

Neutra asked what the inferential consequences were of saying the ALS is due to EMF or that it is due to shock. Does it make any difference, and if so how could you study it to sort that out? Ahlbom noted that it is just the utility workers that are exposed to both these factors. He suggested that studying some other populations would resolve this question. Savitz doubted that there could be another occupational group that is exposed to magnetic fields without shocks.

Sahl suggested comparing linemen (who, he argued do not get electric shock) to substation electricians or generation station electricians (who do). Mayo, a lineman, countered that he frequently got shocked climbing a tower, since the induction creates a potential difference between the person and the steel.

Bowman added that we do not know what magnitude of shocks could be relevant.

Sahl summarized the hypothesis that neurological damage could be due to electrical shocks. He thought that excessive currents down the nerves demyelinate them, which would then cause problems with neurologic functions. However, Carpenter strongly disagreed. He explained that ALS is a degeneration of motor neurons in the spinal cord, but it is not a general spinal cord degeneration. It is a very selective loss of neurons that also affects the neurons in the motor cortex that connect to the spinal cord. In fact, Alzheimer's is also a selective loss of neurons, but different neurons. He thought one is asked to search for some mechanism that promotes the death of very specific nerve cells, a genetically programmed cell death, and many factors that trigger this cell death in different cell types are just those factors that have been discussed in the animal experiments around EMF: elevations of intracellular calcium, free radicals, etc. What nobody understands is why in one disease, it is one type of neuron that goes and in another disease it is a different type. In Parkinson's it is yet a different type.