Overview of the epidemiologic studies on the health effects of ELF magnetic and electric fields published in the first trimester of 2016

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1. <u>Reviews</u>

EFFECTS OF ELECTROMAGNETIC FIELD EXPOSURE ON THE HEART: A SYSTEMATIC REVIEW. Elmas O.

Toxicol Ind Health. 2016;32(1):76-82

The use of electrical devices has gradually increased throughout the last century, and scientists have suggested that electromagnetic fields (EMF) generated by such devices may have harmful effects on living creatures. This work represents a systematic review of collective scholarly literature examining the effects of EMFs on the heart. Although most works describing effects of EMF exposure have been carried out using city electric frequencies (50-60 Hz), a consensus has not been reached about whether long- or short-term exposure to 50-60 Hz EMF negatively affects the heart. Differences between results of studies may be due to a compensatory response developed by the body over time. At greater EMF strengths or shorter exposures, the ability of the body to develop compensation mechanisms is reduced and the potential for heart-related effects increases. It is noteworthy that diseases of heart tissues such as myocardial ischemia can also be successfully treated using EMF.

Conclusions: Despite the substantial volume of data that has been collected on heart-related effects of EMFs, additional studies are needed at the cellular and molecular level to fully clarify the subject.

EXPOSURE TO POWER-FREQUENCY MAGNETIC FIELDS AND THE RISK OF INFERTILITY AND ADVERSE PREGNANCY OUTCOMES: UPDATE ON THE HUMAN EVIDENCE AND RECOMMENDATIONS FOR FUTURE STUDY DESIGNS.

Lewis RC, Hauser R, Maynard AD, Neitzel RL, Wang L, Kavet R, Meeker JD. *J Toxicol Environ Health B Crit Rev. 2016;19(1):29-45.*

Infertility and adverse pregnancy outcomes are significant public health concerns with global prevalence. Over the past 35 years, research has addressed whether exposure to power-frequency magnetic fields is one of the etiologic factors attributed to these conditions. However, no apparent authoritative reviews on this topic have been published in the peer-reviewed literature for nearly 15 years. This review provides an overview and critical analysis of human studies that were published in the peer-reviewed literature between 2002 and July 2015. Using PubMed, 13 epidemiology studies published during this time frame that concern exposure to magnetic fields and adverse prenatal (e.g., miscarriage), neonatal (e.g., preterm birth or birth defects), and male fertility (e.g., poor semen quality) outcomes were identified. Some of these studies reported associations whereas others did not, and study design limitations may explain these inconsistencies. Future investigations need to be designed with these limitations in mind to address existing research gaps. In particular, the following issues are discussed: (1) importance of selecting the appropriate study population, (2) need for addressing confounding due to

unmeasured physical activity, (3) importance of minimizing information bias from exposure measurement error, (4) consideration of alternative magnetic field exposure metrics, and (5) implications and applications of personal exposure data that are correlated within female-male couples.

Conclusions: Further epidemiologic research is needed, given the near ubiquitous exposures to power-frequency magnetic fields in the general population.

2. Residential exposure

NOCEBO RESPONSES TO HIGH-VOLTAGE POWER LINES: EVIDENCE FROM A PROSPECTIVE FIELD STUDY.

Porsius JT, Claassen L, Woudenberg F, Smid T, Timmermans DR. *Sci Total Environ. 2016;543(Pt A):432-328.*

Experimental studies suggest that nocebo responses might occur after exposure to equipment emitting electromagnetic fields such as high voltage power lines (HVPLs) or mobile phone base stations.

The present study investigates to what extent health responses to a new HVPL can be explained by beliefs of residents regarding the health effects of HVPLs.

The authors used a quasi-experimental prospective field study design with two pretests during the construction of a new HVPL, and two posttests after it has been put into operation. Residents living near (0-300m, n=229; 300-500m, n=489) and farther away (500-2000m, n=536) filled out questionnaires about their health and their beliefs about the negative health effects of power lines. Longitudinal mediation models were applied to investigate to what extent these beliefs could explain a change in reported symptoms after the new line was put into operation.

Significant (p<.01) indirect effects were found for proximity on the increase in reported cognitive (R(2)=0.41) and somatic (R(2)=0.79) symptoms after the power line was put into operation through an increase in the belief that power lines causes health effects. The direct effects of proximity on an increase in reported symptoms were not significant.

Conclusions: These findings suggest that increases in reported health complaints after a new HVPL has been put into operation can be explained by nocebo mechanisms. Future field studies are needed to know whether these findings extend to other environmental health issues in a community.

3. Occupational exposure

OCCUPATIONAL EXPOSURE TO MAGNETIC FIELDS AND BREAST CANCER AMONG CANADIAN MEN.

Grundy A, Harris SA, Demers PA, Johnson KC, Agnew DA; Canadian Cancer Registries Epidemiology Research Group, Villeneuve PJ. *Cancer Med.* 2016;5(3):586-596.

Occupational magnetic field (MF) exposure has been suggested as a risk factor for breast cancer in both men and women. Due to the rarity of this disease in men, most epidemiologic studies investigating this relationship have been limited by small sample sizes. Herein, associations of several measures of occupational MF exposure with breast cancer in men were investigated using data from the population-based case-control component of the Canadian National Enhanced Cancer Surveillance System. Lifetime job histories were provided by 115 cases and 570 controls. Average MF

exposure of individual jobs was classified into three categories (<0.3, 0.3 to <0.6, or $\ge 0.6 \ \mu\text{T}$) through expert blinded review of participant's lifetime occupational histories. The impact of highest average and cumulative MF exposure, as well as exposure duration and specific exposure-time windows, on cancer risk was examined using logistic regression. The proportion of cases (25%) with a highest average exposure of $\ge 0.3 \ \mu\text{T}$ was higher than among controls (22%). An elevated risk of breast cancer in men who were exposed to $\ge 0.6 \ \mu\text{T}$ (odds ratio [OR] = 1.80, 95% CI = 0.82-3.95) when compared to those with exposures <0.3 $\ \mu\text{T}$ was found. Those exposed to occupational MF fields for at least 30 years had a nearly threefold increase in risk of breast cancer (OR = 2.77, 95% CI = 0.98-7.82) when compared to those with background levels of exposure. Findings for the other time-related MF variables were inconsistent.

Conclusions: This analysis provides limited support for the hypothesis that exposure to MF increases the risk breast cancer in men.

EFFECTS OF ELECTROMAGNETIC FIELDS EXPOSURE ON PLASMA HORMONAL AND INFLAMMATORY PATHWAY BIOMARKERS IN MALE WORKERS OF A POWER PLANT. Wang Z, Fei Y, Liu H, Zheng S, Ding Z, Jin W, Pan Y, Chen Z, Wang L, Chen G, Xu Z, Zhu Y, Yu Y.

Int Arch Occup Environ Health. 2016;89(1):33-42.

The aim of this study was to evaluate the effects of EMF exposure on levels of plasma hormonal and inflammatory pathway biomarkers in male workers of an electric power plant. Seventy-seven male workers with high occupational EMF exposure and 77 male controls with low exposure, matched by age, were selected from a cross-sectional study. Moreover, high EMF exposure group was with walkie-talkies usage and exposed to power frequency EMF at the work places for a longer duration than control group. A questionnaire was applied to obtain relevant information, including sociodemographic characteristics, lifestyle factors, and EMF exposures. Plasma levels of testosterone, estradiol, melatonin, NF-κB, heat-shock protein (HSP) 70, HSP27, and TET1 were determined by an enzyme-linked immunosorbent assay.

The EMF exposure group had statistically significantly lower levels of testosterone ($\beta = -0.3 \text{ nmol/L}$, P = 0.015), testosterone/estradiol (T/E2) ratio ($\beta = -15.6$, P = 0.037), and NF- κ B ($\beta = -20.8 \text{ ng/L}$, P = 0.045) than the control group. Moreover, joint effects between occupational EMF exposure and employment duration, mobile phone fees, years of mobile phone usage, and electric fees on levels of testosterone and T/E2 ratio were observed. Nevertheless, no statistically significant associations of EMF exposures with plasma estradiol, melatonin, HSP70, HSP27, and TET1 were found.

Conclusions: The findings showed that chronic exposure to EMF could decrease male plasma testosterone and T/E2 ratio, and it might possibly affect reproductive functions in males. No significant associations of EMF exposure with inflammatory pathway biomarkers were found.

4. Human experimental studies

LOW INTENSITY MAGNETIC FIELD INFLUENCES SHORT-TERM MEMORY: A STUDY IN A GROUP OF HEALTHY STUDENTS. Navarro EA, Gomez-Perretta C, Montes F. *Bioelectromagnetics. 2016;37:37-48.*

This study analyses if an external magnetic stimulus (2 kHz and approximately 0.1 µT applied near frontal cortex) influences working memory, perception, binary decision,

motor execution, and sustained attention in humans. A magnetic stimulus and a sham stimulus were applied to both sides of the head (frontal cortex close to temporal-parietal area) in young and healthy male test subjects (n = 65) while performing Sternberg's memory scanning task. There was a significant change in reaction time. Times recorded for perception, sustained attention, and motor execution were lower in exposed subjects (P < 0.01). However, time employed in binary decision increased for subjects exposed to magnetic fields.

Conclusions: It seems that a low intensity 2 kHz exposure modifies short-term working memory, as well as perception, binary decision, motor execution, and sustained attention.

DOES ELECTROMAGNETIC HYPERSENSITIVITY ORIGINATE FROM NOCEBO RESPONSES? INDICATIONS FROM A QUALITATIVE STUDY. Dieudonné M.

Bioelectromagnetics. 2016;37(1):14-24.

Idiopathic Environmental Intolerance attributed to Electromagnetic Fields (IEI-EMF) is a condition in which symptoms are attributed to electromagnetic field (EMF) exposure. As electro-hypersensitive (EHS) people have repeatedly been observed, during provocation trials, to report symptoms following perceived rather than actual exposure, the hypothesis has been put forward that IEI-EMF originates from psychological mechanisms, especially nocebo responses. This paper examines this hypothesis, using data from a qualitative study aimed at understanding how EHS people come to regard themselves as such. Forty self-diagnosed EHS people were interviewed. A typified model of their attribution process was then elaborated, inductively, from their narratives. This model is linear and composed of seven stages: (1) onset of symptoms; (2) failure to find a solution; (3) discovery of EHS; (4) gathering of information about EHS; (5) implicit appearance of conviction; (6) experimentation; (7) conscious acceptance of conviction.

Conclusions: Overall, symptoms appear before subjects start questioning effects of EMF on their health, which is not consistent with the hypothesis that IEI-EMF originates from nocebo responses to perceived EMF exposure. However, such responses might occur at the sixth stage of the process, potentially reinforcing the attribution. It remains possible that some cases of IEI-EMF originate from other psychological mechanisms.

POSSIBLE INFLUENCES OF SPARK DISCHARGES ON CARDIAC PACEMAKERS.

Korpinen L, Kuisti H, Tarao H, Virtanen V, Pääkkönen R, Dovan T, Kavet R. *Health Phys. 2016;110(1):1-10.*

Exposure to spark discharges may occur beneath high voltage transmission lines when contact is initiated with a conductive object (such as a motor vehicle) with the spark discharge mediated by the ambient electric field from the line. The objective of this study was to assess whether such exposures could interfere with the normal functioning of implanted cardiac pacemakers (PMs). The experiment consisted of PMs implanted in a human-sized phantom and then exposed to spark discharge through an upper extremity. A circuit was designed that produced spark discharges between two spherical electrodes fed to the phantom's left hand. The circuit was set to deliver a single discharge per half cycle (every 10 ms) about 10 µs in duration with a peak current of 1.2-1.3 A, thus simulating conditions under a 400-kV power line operating at 50 Hz. Of 29 PMs acquired, all were tested in unipolar configuration and 20 in bipolar

configuration with exposure consisting of 2 min of continuous exposure (one unit was exposed for 1 min).

Conclusions: No interference was observed in bipolar configuration. One unit in unipolar configuration incorrectly identified ventricular extra systoles (more than 400 beats min(-1)) for 2 s. The use of unipolar configuration in new implants is extremely rare, thus further minimizing the risk of interference with the passage of time. Replication of this study and, if safety for human subjects can be assured, future testing of human subjects is also advisable.

5. Exposure assessment

PERSONAL POWER-FREQUENCY MAGNETIC FIELD EXPOSURE IN WOMEN RECRUITED AT AN INFERTILITY CLINIC: ASSOCIATION WITH PHYSICAL ACTIVITY AND TEMPORAL VARIABILITY.

Lewis RC, Hauser R, Wang L, Kavet R, Meeker JD. *Radiat Prot Dosimetry. 2016;168(4):478-488.*

Current epidemiologic approaches for studying exposure to power-frequency magnetic fields and the risk of miscarriage are potentially biased due to lack of attention to the relationship of exposure with physical activity and within-individual variability in exposures over time. This analysis examines these two issues using data from a longitudinal pilot study of 40 women recruited from an infertility clinic that contributed data for up to three 24-h periods separated by a median of 3.6 weeks. Physical activity was positively associated with peak exposure metrics. Higher physical activity within environments did not necessarily lead to higher peak exposures, suggesting that movement between and not within environments increases one's probability of encountering a high field source. Peak compared with central tendency metrics were more variable over time.

Conclusions: Future epidemiology studies associated with peak exposure metrics should adjust for physical activity and collect more than 1 d of exposure measurement to reduce bias.

6. Leukaemia studie

PARENTAL, IN UTERO, AND EARLY-LIFE EXPOSURE TO BENZENE AND THE RISK OF CHILDHOOD LEUKEMIA: A META-ANALYSIS.

Carlos-Wallace FM, Zhang L, Smith MT, Rader G, Steinmaus C. *Am J Epidemiol.* 2016;183(1):1-14.

Benzene is an established cause of adult leukemia, but whether it is associated with childhood leukemia remains unclear. The authors conducted a meta-analysis in which they reviewed the epidemiologic literature on this topic and explored causal inference, bias, and heterogeneity. The exposure metrics that were evaluated included occupational and household use of benzenes and solvents, traffic density, and traffic-related air pollution. For studies of occupational and household product exposure published from 1987 to 2014, the summary relative risk for childhood leukemia was 1.96 (95% confidence interval (CI): 1.53, 2.52; n = 20). In these studies, the summary relative risk was higher for acute myeloid leukemia (summary relative risk (sRR) = 2.34, 95% CI: 1.72, 3.18; n = 6) than for acute lymphoblastic leukemia (sRR = 1.57; 95% CI: 1.21, 2.05; n = 14). The summary relative risk was higher for maternal versus paternal exposure, in studies that assessed benzene versus all solvents, and in studies of

gestational exposure. In studies of traffic density or traffic-related air pollution published from 1999 to 2014, the summary relative risk was 1.48 (95% CI: 1.10, 1.99; n = 12); it was higher for acute myeloid leukemia (sRR = 2.07; 95% CI: 1.34, 3.20) than for acute lymphoblastic leukemia (sRR = 1.49; 95% CI: 1.07, 2.08) and in studies that involved detailed models of traffic pollution (sRR = 1.70; 95% CI: 1.16, 2.49).

Conclusions: Overall, evidence of associations between childhood leukemia and several different potential metrics of benzene exposure were identified.

TRAFFIC-RELATED AIR POLLUTION AND CHILDHOOD ACUTE LEUKEMIA IN OKLAHOMA.

Janitz AE, Campbell JE, Magzamen S, Pate A, Stoner JA, Peck JD. *Environ Res. 2016;148:102-111.*

Ambient air pollution has been classified as a Group 1 carcinogen, but studies have not established whether traffic-related air pollution is associated with leukemia. The goal of this study was to determine if children with acute leukemia had higher odds of exposure to traffic-related air pollution at birth compared to controls.

The authors conducted a case-control study using the Oklahoma Central Cancer Registry to identify cases of acute leukemia in children diagnosed before 20 years of age between 1997 and 2012 (n=307). Controls were selected from birth certificates and matched to cases on week of birth (n=1013). Using a novel satellite-based land-use regression model of nitrogen dioxide (NO2) and estimating road density based on the 2010 US Census, the association between traffic-related air pollution and childhood leukemia was evaluated using conditional logistic regression.

The odds of exposure to the fourth quartile of NO2 (11.19-19.89ppb) were similar in cases compared to controls after adjustment for maternal education (OR: 1.08, 95% CI: 0.75, 1.55). These estimates were stronger among children with acute myeloid leukemia (AML) than acute lymphoid leukemia, with a positive association observed among urban children with AML (4th quartile odds ratio: 5.25, 95% confidence interval: 1.09, 25.26). While no significant association was observed with road density, male cases had an elevated odds of exposure to roads at 500m from the birth residence compared to controls (OR: 1.39, 95% CI: 0.93, 2.10), which was slightly attenuated at 750m.

Conclusions: Although no association was observed between NO2 or road density, this was the first study to observe an elevated odds of exposure to NO2 among children with AML compared to controls, suggesting further exploration of traffic-related air pollution and AML is warranted.

RESIDENTIAL MOBILITY AND THE RISK OF CHILDHOOD LEUKEMIA. Järvelä L, Raitanen J, Erme S, Lohi O, Auvinen A. *Cancer Causes Control. 2016;27(3):433-443.*

An infective origin of childhood leukemia has been postulated, with leukemia developing as a rare response to an infection. Population mixing can result in increased contacts between infected and susceptible individuals and may increase the risk of leukemia. The objective of this study was to investigate the association between residential mobility as an indicator of population mixing at individual level and the risk of leukemia in children (<15 years).

The authors conducted a population-based case-control study using Finnish register data. Cases (n = 1,093) were all children diagnosed with leukemia (M9800-M9948 in ICD-O-3) at <15 years of age in Finland in 1990-2011. Randomly three controls per case (n = 3,279), free of cancer and alive in the end of the index year (diagnosis of the case) were chosen. Controls were matched by sex and age. A comprehensive history of residential mobility was constructed from the population registry including overall migration, moving to a larger municipality (more inhabitants), and moving to a municipality with low, intermediate, or high migration intensity. The association between residential mobility and the risk of childhood leukemia was evaluated using conditional logistic regression.

The authors did not observe consistently increased or decreased risks of childhood leukemia associated with different migration patterns. Overall, residential mobility showed odds ratios non-significantly below unity, and no elevated risks were found.

Conclusions: These results do not indicate that higher residential mobility or moving to municipalities with more inhabitants is associated with risk of childhood leukemia.