Dr. Maurits De Ridder Occupational and Environmental Health Section Ghent University

1. Reviews

EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS STIMULATION MODULATES AUTOIMMUNITY AND IMMUNE RESPONSES: A POSSIBLE IMMUNO-MODULATORY THERAPEUTIC EFFECT IN NEURODEGENERATIVE DISEASES. Guerriero F, Ricevuti G. *Neural Regen Res.* 2016;11(12):1888-1895.

Increasing evidence shows that extremely low frequency electromagnetic fields (ELF-EMFs) stimulation is able to exert a certain action on autoimmunity and immune cells. In the past, the efficacy of pulsed ELF-EMFs in alleviating the symptoms and the progression of multiple sclerosis has been supported through their action on neurotransmission and on the autoimmune mechanisms responsible for demyelination. Regarding the immune system, ELF-EMF exposure contributes to a general activation of macrophages, resulting in changes of autoimmunity and several immunological reactions, such as increased reactive oxygen species-formation, enhanced phagocytic activity and increased production of chemokines. Transcranial electromagnetic brain stimulation is a non-invasive novel technique used recently to treat different neurodegenerative disorders, in particular Alzheimer's disease. Despite its proven value, the mechanisms through which EMF brain-stimulation exerts its beneficial action on neuronal function remains unclear. Recent studies have shown that its beneficial effects may be due to a neuroprotective effect on oxidative cell damage. On the basis of in vitro and clinical studies on brain activity, modulation by ELF-EMFs could possibly counteract the aberrant pro-inflammatory responses present in neurodegenerative disorders reducing their severity and their onset. The objective of this review is to provide a systematic overview of the published literature on EMFs and outline the most promising effects of ELF-EMFs in developing treatments of neurodegenerative disorders.

Conclusions: Reviewed data are supporting the role of ELF-EMF in generating immune-modulatory responses, neuromodulation, and potential neuroprotective benefits. Nonetheless, the underlying mechanisms of interaction between EMF and the immune system are still to be completely understood and need further studies at a molecular level.

2. <u>Residential exposure</u>

"THESE POWER LINES MAKE ME ILL": A TYPOLOGY OF RESIDENTS' HEALTH RESPONSES TO A NEW HIGH-VOLTAGE POWER LINE. Porsius JT, Claassen, Woudenberg F, Smid T, Timmermans DR. *Risk Anal. 2017 Mar 17.*

Little attention has been devoted to the potential diversity in residents' health responses when exposed to an uncertain environmental health risk. The present study explores whether subgroups of residents respond differently to a new high-voltage power line (HVPL) being put into operation. 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 was put into operation. Residents living nearby (0-300 m, n = 229) filled out questionnaires about their health and their perception of the environment. Latent class growth models were applied to investigate heterogeneity in the belief that health complaints were caused by a power line. Classes were compared on a wide range of variables relating to negative-oriented personality traits, perceived physical and mental health, and perceptions of the environment. The authors identified five distinct classes of residents, of which the largest (49%) could be described as emotionally stable and healthy with weak responses to the introduction of a new power line. A considerable minority (9%) responded more strongly to the new line being activated. Residents in this class had heard more about the health effects of power lines beforehand, were more aware of the activation of the new line, and reported a decrease in perceived health afterwards.

Conclusions: The authors conclude that there is a considerable heterogeneity in health responses to a new HVPL. Health risk perceptions appear to play an important role in this typology, which has implications for risk management.

3. Human experimental studies

EFFECTS OF PERSONALISED EXPOSURE ON SELF-RATED ELECTROMAGNETIC HYPERSENSITIVITY AND SENSIBILITY - A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL.

van Moorselaar I, Slottje P, Heller P, van Strien R, Kromhout H, Murbach M, Kuster N, Vermeulen R, Huss A. *Environ Int.* 2017;99:255-262.

Previous provocation experiments with persons reporting electromagnetic hypersensitivity (EHS) have been criticised because EHS persons were obliged to travel to study locations (seen as stressful), and that they were unable to select the type of signal they reported reacting to. In this study the authors used mobile exposure units that allow double-blind exposure conditions with personalised exposure settings (signal type, strength, duration) at home. The aim was to evaluate whether subjects were able to identify exposure conditions, and to assess if providing feedback on personal test results altered the level of self-reported EHS.

A double-blind randomised controlled exposure testing with questionnaires was used at baseline, immediately before and after testing, and at two and four months post testing. Participants were eligible if they reported sensing either radiofrequency or extremely low frequency fields within minutes of exposure. Participants were visited at home or another location where they felt comfortable to undergo testing. Before double-blind testing, the authors verified together with participants in an unblinded exposure session that the exposure settings were selected were ones that the participant responded to. Double-blind testing consisted of a series of 10 exposure and sham exposures in random sequence, feedback on test results was provided directly after testing.

42 persons participated, mean age was 55 years (range 29-78), 76% were women. During double-blind testing, no participant was able to correctly identify when they were being exposed better than chance. There were no statistically significant differences in the self-reported level of EHS at follow-up compared to baseline, but during follow-up participants reported reduced certainty in reacting within minutes to exposure and reported significantly fewer symptoms compared to baseline.

Conclusions: These results suggest that a subgroup of persons exist who profit from participation in a personalised testing procedure.

4. Exposure assessment

MEASUREMENTS OF INTERMEDIATE-FREQUENCY ELECTRIC AND MAGNETIC FIELDS IN HOUSEHOLDS.

Aerts S, Calderon C, Valič B, Maslanyj M, Addison D, Mee T, Goiceanu C, Verloock L, Van den Bossche M, Gajšek P, Vermeulen R, Röösli M, Cardis E, Martens L, Joseph W. *Environ Res. 2017;154:160-170.*

Historically, assessment of human exposure to electric and magnetic fields has focused on the extremely-low-frequency (ELF) and radiofrequency (RF) ranges. However, research on the typically emitted fields in the intermediate-frequency (IF) range (300Hz to 1MHz) as well as potential effects of IF fields on the human body remains limited, although the range of household appliances with electrical components working in the IF range has grown significantly (e.g., induction cookers and compact fluorescent lighting). In this study, an extensive measurement survey was performed on the levels of electric and magnetic fields in the IF range typically present in residences as well as emitted by a wide range of household appliances under real-life circumstances. Using spot measurements, residential IF field levels were found to be generally low, while the use of certain appliances at close distance (20 cm) may result in a relatively high exposure. Overall, appliance emissions contained either harmonic signals, with fundamental frequencies between 6kHz and 300kHz, which were sometimes accompanied by regions in the IF spectrum of rather noisy, elevated field strengths, or much more capricious spectra, dominated by 50Hz harmonics emanating far in the IF domain. The maximum peak field strengths recorded at 20 cm were 41.5V/m and 2.7A/m, both from induction cookers.

Conclusions: None of the appliance emissions in the IF range exceeded the exposure summation rules recommended by the International Commission on Non-Ionizing Radiation Protection guidelines and the International Electrotechnical Commission (IEC 62233) standard at 20 cm and beyond (maximum exposure quotients EQE 1.0 and EQH 0.13).

5. Leukaemia studie

HOME REMODELING AND RISK OF CHILDHOOD LEUKEMIA.

Whitehead TP, Adhatamsoontra P, Wang Y, Arcolin E, Sender L, Selvin S, Metayer C.

Ann Epidemiol. 2017;27(2):140-144.e4.

The authors investigated the relationship between the risk of childhood leukemia and home remodeling, a surrogate for indoor chemical exposures. They collected information on remodeling activities carried out between birth and diagnosis in homes of 609 acute lymphoblastic leukemia (ALL) cases, 89 acute myeloid leukemia (AML) cases, and 893 matched controls participating in the California Childhood Leukemia Study (1995-2008). Multivariable logistic regression was used to estimate the risk of ALL and AML associated with six remodeling activities: construction, painting, recarpeting, reflooring, roofing, and weatherproofing. Models were adjusted for age, sex, Hispanic ethnicity, race, household annual income, and residential mobility.

Construction in the home between birth and diagnosis was associated with a significant increase in ALL risk (odds ratio [OR]: 1.52, 95% confidence interval [CI]: 1.14-2.02) and a nonsignificant increase in AML risk (OR: 1.75, 95% CI: 0.98-3.15). No other remodeling activities were associated with ALL or AML risk in the main analysis. When stratifying by Hispanic ethnicity, a positive relationship between ALL risk and painting was evident in Hispanic children (OR: 1.47, 95% CI: 1.04-2.07).

Conclusions: Specific home remodeling activities appeared to be associated with increased risk of childhood ALL.

A TASK-BASED ASSESSMENT OF PARENTAL OCCUPATIONAL EXPOSURE TO PESTICIDES AND CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA. Gunier RB, Kang A, Hammond SK, Reinier K, Lea CS, Chang JS, Does M, Scelo G, Kirsch J, Crouse V, Cooper R, Quinlan P, Metayer C. *Environ Res.* 2017;156:57-62.

The authors assessed parental occupational pesticide exposure from the year before pregnancy to the child's third year of life for 669 children diagnosed with ALL and 1021 controls. Expert rating using task-based job modules (JM) was conducted to estimate exposure to pesticides among farmer workers, gardeners, agricultural packers, and pesticide applicators. This method was compared to (1) partial JM using job titles and a brief description, but without completing the task-based questionnaire, and (2) job exposure matrix (JEM) linking job titles to the International Standard Classifications of Occupation Codes. Unconditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for ALL cancer risk and pesticide exposure adjusting for child's sex, age, race/ethnicity and household income.

Compared to complete JMs, partial JMs and JEM led to 3.1% and 9.4% of parents with pesticide exposure misclassified, respectively. Misclassification was similar in cases and controls. Using complete JMs, an increased risk of ALL was observed for paternal occupational exposure to any pesticides (OR=1.7; 95% CI=1.2, 2.5), with higher risks reported for pesticides to treat nut crops (OR=4.5; 95% CI=0.9, 23.0), and for children diagnosed before five years of age (OR=2.3; 95% CI: 1.3, 4.1). Exposure misclassification from JEM attenuated these associations by about 57%. Maternal occupational pesticide exposure before and after birth was not associated with ALL.

Conclusions: The risk of ALL was elevated in young children with paternal occupational pesticide exposure during the perinatal period, using more detailed occupational information for exposure classification.

RESIDENTIAL PROXIMITY TO GASOLINE STATIONS AND RISK OF CHILDHOOD LEUKEMIA. Infante PF. *Am J Epidemiol. 2017;185(1):1-4.*

Significant elevations in the risk of childhood leukemia have been associated with environmental exposure to gasoline; aromatic hydrocarbons from refinery pollution, petroleum waste sites, and mobile sources (automobile exhaust); paints, paint products, and thinners; and secondary cigarette smoke in the home. These higher risks have also been associated with parental exposure to benzene, gasoline, motor vehicle-related jobs, painting, and rubber solvents.

Conclusions: These exposures and jobs have 1 common chemical exposure-benzene, a recognized cause of acute leukemia in adults-and raise the question of whether

children represent a subpopulation in which a higher risk of leukemia is associated with very low level exposure to environmental benzene.

IN UTERO CYTOMEGALOVIRUS INFECTION AND DEVELOPMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.

Francis SS, Wallace AD, Wendt GA, Li L, Liu F, Riley LW, Kogan S, Walsh KM, de Smith AJ, Dahl GV, Ma X, Delwart E, Metayer C, Wiemels JL. *Blood.* 2017;129(12):1680-1684.

It is widely suspected, yet controversial, that infection plays an etiologic role in the development of acute lymphoblastic leukemia (ALL), the most common childhood cancer and a disease with a confirmed prenatal origin in most cases. The authors investigated infections at diagnosis and then assessed the timing of infection at birth in children with ALL and age, gender, and ethnicity matched controls to identify potential causal initiating infections. Comprehensive untargeted virome and bacterial analyses of pretreatment bone marrow specimens (n = 127 ALL in comparison with 38 acute myeloid leukemia cases in a comparison group) revealed prevalent cytomegalovirus (CMV) infection at diagnosis in childhood ALL, demonstrating active viral transcription in leukemia blasts as well as intact virions in serum. Screening of newborn blood samples revealed a significantly higher prevalence of in utero CMV infection in ALL cases (n = 268) than healthy controls (n = 270) (odds ratio [OR], 3.71, confidence interval [CI], 1.56-7.92, P = .0016). Risk was more pronounced in Hispanics (OR=5.90, CI=1.89-25.96) than in non-Hispanic whites (OR=2.10 CI= 0.69-7.13).

Conclusions: This is the first study to suggest that congenital CMV infection is a risk factor for childhood ALL and is more prominent in Hispanic children. Further investigation of CMV as an etiologic agent for ALL is warranted.