THESES OF PH.D. DISSERTATION

Animal and human studies of the behavioral and phisiological effects of extremely low frequency electromagnetic field exposure

Renáta Szemerszky

Supervisor: prof Dr. György Bárdos

full professor, Doctor of Hungarian Academy of Sciences

Eötvös Loránd University

Biology Ph.D. School

Head: prof Dr. Anna Erdei, DSc., full member of HAS

Neurosciences- and Human Biology Ph.D. Program

Head of the Program: prof Dr. László Détári, DSc.

ELTE Department of Phisiology and Neurobiology

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Introduction

A typical feature of our age is that introduction of new technologies serving our convenience and – directly or indirectly – our health is always accompanied by new complaints, fears, and worries (Petrie és mtsai 2005), i. e. with the improvement of the quality of life the feeling of personal vulnerability is increasing (paradox of health; Barsky 1988). One of the most typical representatives of harmful environmental influences is the increasing electromagnetic (EM) pollution, therefore its effect on human health is an important topic. Electromagnetic hypersensitivity or electrosensitivity (EHS), a phenomenon described 40 years ago in Northern Europe, refers to the proneness to experience discomfort and non-specific symptoms in the proximity of functioning electrical devices. The phenomenon is quite heterogenous regarding the types of reported symptoms (various complaints affecting the skin and the central nervous system, e.g. crawl, burning sensations and drowsiness, headache, respectively) as well as regarding the triggering sources (e.g. power lines, monitors, microwave owens, mobile phones).

Although the increasing prevalence of EHS entails a considerable financial burden on the health care system of the affected countries (Stenberg 2004), the question of its background is yet to be clarified scientifically. On one hand, a small proportion of the population may be sensitized against environmental factors by certain biophysical-biochemical characteristics. On the other hand, the phenomenon may be of psychological as opposed to biological origin and its development may be facilitated by certain personality traits and psychosocial factors. The first possibility is called *toxicogenic* (i.e. biological) theory, while the second one is referred to as *psychogenic* (i.e. psychological) theory. The appropriate therapy of electromagnetic hypersensitivity depends heavily on its background which makes the question of background mechanism quite important (Rubin et al. 2005).

Goals

Our work has aimed at the complex investigation of possible toxicogenic and psychogenic background of the EHS phenomenon. In our animal experiments, symptoms evoked by EM fields (EMFs) were modelled free of human psychosocial factors in adult male Wistar rats. In our human work, the psychological aspects of the EHS phenomenon and combined effects of psychogenic and toxicogenic factors were studied. Our goals were as follows.

1. Developing an animal behavior monitoring system and using a multivariate statistical method which makes it possible to avoid the methodological and statistical pitfalls that are characteristic of this area of research and that often lead to contradictory findings.

2. To study the behavioral effects of EMF exposures of various magnetic induction (0.5 and 3 mT) and of various duration (20 minutes, eight ours, one week, six weeks) in adult male Wistar rats using the validated behavior

monitoring system and statistical method. To reveal the possible dose-response relationship as a function of magnitude and of duration of exposure.

3. In human studies, to describe of symptoms attributed to EM fields and of personality traits that make people prone to symptom generation.

4. To demonstrate the nocebo-effect by sham EMF exposure (i.e. under circumstances that are free of possible biological effects). To study the causal relationships between symptom generation and potential psychosocial factors.

5. Complex modelling of psychogenic and toxicogenic background of EHS in actual EMF exposure. To investigate possible relationships between electrosensitivity (EHS) and enchaced detection ability (electrosensibility).

Procedures

- Animal experiments using a behavior-oriented monitoring system consisting of three widely used animal models (elevated plus maze - EPM, social avoidance - SA, open field test - OF).
- Analysis of data obtained from the three behavioral tests using exploratory factor analysis in order to reveal latent structure of behavior. Creation of composite variables to reduce the high number of elementary behavioral variables. Demonstration of the utility of the method by testing the behavioral effects of m-CPP (meta-chlorophenilpiperazine).
- Investigation of the effects of various EMF exposures using a systematic research protocol and testing parameters. Demonstrating the reliability of the results by calculating statictical power and effect size. Meta-analysis of data obtained from various EMF exposures in order to improve reliability of results.
- Testing of sucrose preference and measuring changes of body weight during chronic EM exposure.
- In human studies, applying of double-blind, computer-guided human experimental protocols during sham- and actual EMF exposures.
- By applying validated psychological scales, assessing subjective body symptoms (PHQ-15), trait anxiety (STAI-T), state anxiety (STAI-S), satisfaction with life (SWLS), dispositional optimism (LOT-R), somatosensory amplification (SSAS), and modern health worries (MHW).
- Analysis of detection ability of EM fields by a method based on the Signal Detection Theory.
- Analysis of heart rate (HR) and heart rate variabilty using various indices (SDNN, HF, LF, LF/HF) from human ECG records using the modified Lead II electrode placement.
- Multiple regression analyses and path analysis in order to expore relationships among variables.

Results (Theses)

1. **As far as the animal models are concerned, the use of general interpretation schemas for the explanation of behavior is not appropriate, adaptation of the tests to the particular experimental situation and to the experimental protocol and validation of the results are always necessary**

Three latent components of behavior were identified by exploratory factor analysis in the selected animal models. Loadings of behavioral elements on the factors differed from what we had expected based on general ethological interpretation schemata. It was demonstrated that behavioral models are particularly sensitive to changes of testing conditions. In other words, meaning and importance of elementary components of behavior are not stable even in the same context. The number of behavioral elements were reduced by creating composite variables representing latent factors of behavior, which enabled us to reduce likelihood of statistical errors and to evaluate behavior in its complexity. Moreover, were had became able to interpret variables on an empirical basis instead of using an a priori theoretical interpretation.

2. **As 50 Hz electromagnetic field exposure of various magnitude and duration had not have a measurable impact on the behavior of rats, toxicogenic (biological) origin of the EHS phenomenon were not supported by our data**

Classical analysis based on comparing elementary components of behavior had not lead to interpretable results. Positive (statistically significant) results were not acceptable as their proportion were nearly identical (~ 5%) to the proportion of Type I statictical error, whereas negative (non-significant) results were not acceptable because of their too low statistical power (too high Type II error). The issue was resolved by using composite variables which enabled us to reduce the number of statistical tests and of Type I error, making the interpretation more reliable. This second analysis revealed no dose-response relationship. Similarly, meta-analysis of our data have not yielded positive results. Neither locomotor, anxiety mediated nor social behavior had been altered by any EMF exposure in male Wistar rats. Lack of changes in behavior may reflect to lack of changes in physical, emotional, and motivational state of the animals. Therefore, the toxicogenic approach has not been supported by data from animal models of social avoidance, proneness to anxiety, and of general discomfort caused by non-specific symptoms, that are characteristics to people with EHS (Bergdahl 1995). Considering the complexity of our analysis, these results can be regarded reliable.

3. **According to the findings of human studies, complaints of people considering themselves as hypersentitive seem to be non-specific symptoms. Typical personality characteristics are enchanced proneness to somatisation and to somatosensory amplification**

Typically, non-specific symptoms are attributed to EMF exposure. The most often mentioned symptoms are associated with the central nervous system (e.g., headache, fatigue), with sensory functions (e.g., blurred vision, tinnitus), and with the skin (e.g., crawl, sweating), respectively. Experience of symptoms attributed to the EMF were

associated with somatisation tendency (the tendency to experience emotional distress as somatic symptoms; Spinhoven and van der Does 1997) and to somatosensory amplification (experience of body sensations as intense, harmful and disturbing; Barsky et al. 1988). These personality characteristics are also connected to the nocebo-reaction.

4. **Believed presence of EMF leads to production of symptoms and/or to misattribution of symptoms. The extent of nocebo reaction is exaggerated by a negative attitude toward and by concerns about EMF exposure, by higher percieved risk (believed higher magnitude of the exposure), and by certain personality characteristics. These findings support the mainly psychogenic origin of the EHS phenomenon**

Participants considering themselves as hypersensitive expected more symptoms before the EMF exposure and actually experienced more symptoms during or after the exposure. Sham exposure evoked surprisingly high number of symptoms in the EHS group as well as in the control group and higher believed magnitude led to heightened symptom generation. These findings support that EMFs are associated with harmful effects in the people's mind. Moreover, perceived symptoms might be consequences of a nocebo reaction also in real-life situations. In this context, nocebo-effects are non-specific symptoms that cannot be explained by biophysical-biochemical effects of EMFs. Reliable predictors of EHS were concerns about negative health-related effects of EMFs (as assessed by the *Radiation* subscale of the MHW scale), previous expectations of symptoms, somatisation tendency and somatosensory amplification tendency (*PHQ-15* and *SSAS* scale, respectively).

5. **People with EHS as opposed to controls were able to detect the presence of EMF to some extent. Considering this finding, interaction between toxicogenic and psychogenic effects is also possible**

Association between EHS and detection ability of EM fields (electrosensibility, ES) were revealed: people with EHS were able to detect the presence of EMF (50 Hz; 0,5 mT) to some extent. According to the results of HRV-analysis, better detection performance was associated with elevated parasympathetic activity (larger values of HF index). A possible explanation for this finding is that a more relaxed state allows better allocation of attention which leads to better detection performance.

Conclusions

Non-specific symptoms are usually considered as amplified signals of normal body processes or as somatic concomitants of emotions or of stress (Barsky és mtsai 2002). One of the most fundamental human motivations is understanding and controlling the internal as well as the external environment. This motivation plays an essential role in the attribution process: one tries to find an acceptable cause of unpleasant body feelings (Petrie et al. 2001;

Köteles et al. 2011). The final, non-conscious choice depends on the social-cultural milieu as well as on previous experiences and beliefs. This process is called 'labelling' or – more generally – false attribution (Schachter and Singer 1962; Mechanic 1972). Too much attention is paid to possible harmful environmental agents nowadays, and perceived threat posed by these agents is also often exaggerated (Petrie et al. 2001; Petrie and Wessely 2002). The associated negative expectations and concerns make them ideal subjects for the attribution process.

The attribution process evokes increased introspection in the proximity of the supposedly harmful environmental agents which leads to amplification of somatic signals. Amplified signals would be interpreted as symptoms which generates worrying and rumination (Brown 2006) which in turn reinforce the generation of more symptoms in people who are prone to somatisation. Individuals with heightened somatosensory amplificaton tendency experience body signals more intense and disturbing (Barsky 1979; Barsky et al. 1990). Somatosensory amplification can be conceptualized as a non-conscious cognitive-emotional reaction to perceived symptoms or a specific cognitive bias (Mailloux and Brener 2002). EHS people with elevated proneness to somatisation and to somatosensory amplification experience more complaints and more disturbing symptoms which evokes increased tendency to attribution. The process obviously includes not only subjective experiencing of symptoms but also their neurobiological and physiological correlates, therefore it results in worse health status, in higher prevalence of medically unexplained symptoms, and in elevated anxious reaction to symptoms in people with EHS.

Psycho-social and environmental agents can also interact which makes the understanding of the phenomenon more difficult. According to our results, the possibility that EHS people are (at least subliminarly) able to detect the presence of EMF cannot be rejected. Although the magnitude of the EMF was not enough for conscious perception of presence of EMF, subliminary stimuli might have an effect on mood and on general body feelings (Ádám 1998). Negative affect is one of the most important determinant of symptom generation (Aronson et al. 2006; Pennebaker 1994). Moreover, as EMFs evoke anxiety and worrying in people with EHS, a sensitization process might take place which lowers perception threshold just like biofeedback and other learning methods. Lower perception threshold means perception of more symptoms which in turn evokes more anxiety and worrying, leading to a vicious circle. Sensitization can also lead to elevated physiological sensitivity to the effects of EMFs.

In summary, importance of toxicogenic factors in the development and maintenance of EHS is still questionable. According to our findings, however, the psychogenic nocebo effect is always present and plays a more important role in production of symptoms attributed to artificial EMFs than the possible toxicogenic factors.

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