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Effect of radiofrequency exposure emitted by third and fourth generation mobile phones on temperature pain threshold and cognitive functions

PhD Thesis

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Introduction

The electromagnetic load of our environment is mainly derived from artificial sources. Due to the currently ongoing explosive development of telecommunication, cell phone usage has become increasingly common throughout the world. According to some estimates [Kenechi Okeleke, 2017], nearly three quarters of the world's population will be a mobile phone user by 2020. When people use their mobile phones (MPs) directly near the head, a large part of the output radiofrequency (RF) power is absorbed by the head [Gandhi, 2002]. As a consequence, there is a growing concern about the effects of RF radiation emitted by mobile phones on brain function. Nevertheless, we have scarce research available on the potential effects of the newly-developed technological standards on brain function. As most of the available research data are related to the effects of previous technologies (e.g., Global System for Mobile Communications, GSM), and their results are rather contradictory, there is a growing need to investigate the possible neurophysiological and cognitive effects of RF radiation generated by current MP technologies (third generation, 3G; fourth generation, 4G). According to a comprehensive WHO report [WHO, 2006], the relatively low health risk of mobile phones can still have public health implications due to the size of the affected population.

Indeed, a small portion of the population is known to report non-specific, unpleasant symptoms attributed to different types of RF exposure [Rubin et al., 2005]. However, the adverse effects on well-being and the symptoms have not been unambiguously proven to be related to the RF exposure itself, except for the pain associated with the elevated temperature at the site of exposure in the case of high exposure levels [Walters et al., 2000].

However, studies analysing the frequency components of the EEG (electroencephalograph) signal reflecting the brain’s electric activity have demonstrated that the alpha band (8-12 Hz) of the awake EEG is affected by the RF exposure even below the recommended energy exposure level (2 W/kg specific absorption rate, SAR), without clear evidence supporting that any short-term acute effects would be harmful and could pose a general health risk [ICNIRP, 2018b].

Aims

The primary aim of this work was to investigate the effects of acute RF exposure emitted by mobile phone signal systems of the 3G or UMTS (Universal Mobile Telecommunication System) and 4G or LTE (Long Term Evolution) technologies on the central nervous system of healthy young people. The following specific aims were set:

- Does acute UMTS and LTE MP-like exposure affect neurophysiological function indexed by temperature pain threshold as measured in a validated capsaicin-treatment protocol?
- Does acute UMTS and LTE MP-like exposure affect cognitive processes indexed by the so called 'Stroop-effects' in a simple go-no-go cognitive task?
- Does acute UMTS and LTE MP-like exposure affect the alpha band power of the resting state EEG signal?

Materials and Methods

Exposure systems

A precisely controlled UMTS signal was emitted by a system which was previously developed in our laboratories [Parazzini et al., 2009; Stefanics et al., 2008; Trunk et al., 2015; Trunk et al., 2013], while the LTE exposure system was newly developed by us and was first used in the present series of studies. The source of UMTS was powered by a Nokia 6650 (Nokia, Espoo, Finland) mobile phone controlled by the Phoenix service software, while the LTE signal was emitted by a programmable Anritsu MG3700A signal generator (Anritsu Co., Japan) and was further amplified to the desired exposure level. The UMTS exposure operated at 1947 MHz, the LTE at 1750 MHz carrier frequency. On both systems the output signal was transmitted by a patch antenna positioned over the ear to mimic normal cell phone use. For both technologies (UMTS, LTE), exposure parameters (1.8 W/kg SAR) were chosen to approach the public exposure limits recommended by the ICNIRP [ICNIRP, 2018a] (2 W/kg SAR head only exposure).

Thermal pain thresholds measurements

A special thermal stimulator device (Metron Avionics, Pécs) was used to measure the thermal pain threshold (TPT) on the volunteers' fingertips. The device was designed to simultaneously heat the skin and measure its temperature. The heating pads of device were attached to the volunteers' fingertips and elevated the skin temperature until the moment when volunteers felt thermal pain and moved their hand to interrupt the heat rise. The temperature measured by the device at the moment of the hand movement response was defined as the TPT. The pain threshold measurement protocol was previously validated in our laboratory in a capsaicin-induced hyperalgesia protocol on 20 healthy university students (14 females, aged: 22±3 years). Measurement conditions after the validation were the same in the

UMTS and LTE studies: the temperature was increased with a rate of 5 °C/s from 35 °C up to max. 55 °C. Volunteers (healthy university students; UMTS experiment: 22 adults (10 females, aged 22±3 years); LTE experiment: 18 adults (12 females, aged 21±2 years) participated in two experimental sessions in a randomized, double-blind study design. They received real exposure in one session and sham exposure in the other. In each experimental session, TPT was measured in five blocks: one block before the exposure (Pre), one at the beginning and one at the end of the 30-minute RF exposure (Mid), and 30 and 60 minutes after (Post) exposure.

Stroop-effects and resting EEG

The UMTS and LTE experiments were performed with similar measurement settings. Volunteers were healthy university students (UMTS experiment: n=34 (20 females, aged 20±3 years); LTE experiment: n=26 (13 females, aged 21±3 years). In both experiments, after completing the first Stroop test (Pre), non-invasive scalp EEG was continuously recorded for 30 minutes. After the first five minutes of EEG recording (Pre) 20 minutes RF exposure (real/sham) was applied (Mid), and the EEG recording was continued for further 5 minutes after turning off the exposure device (Post). Then, participants performed in a second Stroop test (Post).

The Stroop test measures various higher-order cognitive functions like selective attention, cognitive flexibility, processing speed and executive functions. The main endpoint variables of the Stroop test are the so-called Stroop-effects, which reflect semantic interference (IF) and facilitation (FAC) in different conditions. The Stroop-effects were computed by analysing button press responses to stimuli (reaction times, RTs) in two task variants: Colour Naming (CN) and Word Naming (WN). In the CN task one had to react to the colour of the word (response by shade) and in the WN task one had to establish the meaning of the word (response by meaning). The stimuli used in the Stroop test were the words "red", "green", "blue", or "yellow" written in different colours, with equal number of stimuli shown in each task (WN, CN) and condition (congruent: colour and word meaning were the same, incongruent: colour and word meaning differed, neutral: neither the colour nor the word were among the targets). To test the effects of RF exposure, RT data were subjected to repeated measures of ANOVAs (rANOVA). Two separate analyses were conducted for IF and for FAC, using within-subject factors *Exposure* (Real, Sham) × *Time* (Pre, Post) × *IF* (CN incongruent, CN neutral) or × *FAC* (CN congruent, CN neutral) respectively, with between-subject factor: *RF type* (UMTS, LTE).

Scalp EEG was recorded on 32 channels with passive electrodes placed on the skull according to the international 10-20 system. Impedance was kept below 5 kOhm. The sampling rate of 1 kHz was used. EEG data were analysed using EEGLab 14.0.0b52 in the MATLAB software environment (Mathworks Inc., Natick, MA, USA). Continuous EEG data were cut into three consecutive segments: Pre block (5 min before exposure), Mid block (during exposure, 20 min) and Post block (5 min after exposure). Fast Fourier Transforms (FFTs) with 1 Hz resolution were applied on filtered, artefact-free, epoched (2s, non-overlapping) data, and spectral power was studied in the alpha (8-12 Hz) band. Exposure effects were first analysed on pooled data of the two RF types, then separate analyses were performed for UMTS and LTE exposure. Parametric hypothesis testing (rANOVA) was applied for statistical analyses.

Results

Results of thermal pain threshold measurements

Our TPT measurement method was successfully validated, as acute temperature pain sensitivity appeared as a result of topical capsaicin treatment (main effect of capsaicin *Treatment* $F_{1,18} = 8.450$, $p = 0.009$, $\eta^2_p = 0.319$).

The results of the ANOVAs examining UMTS (Mid) blocks indicated that desensitization occurred ($F_{1.4,28.3} = 138.25$, $p < .001$, $\eta^2_p = 0.868$) during the *Trial*s, which was more pronounced for UMTS (marg. sig. *Exposure* × *Trial* interaction: $F_{1.2,25.7} = 3.014$, $p = 0.088$, $\eta^2_p = 0.126$) than for sham exposure. When TPT was measured on the side contralateral to the exposure, real UMTS exposure induced stronger TPT desensitization compared to sham exposure (*Exposure* × *Trial* interaction on the contralateral side: $F_{1.2,24.6} = 4.304$, $p = 0.043$, $\eta^2_p = 0.170$). There was neither a main effect of exposure nor any interaction in the post-exposure blocks.

Analysing the Mid and Post blocks in the LTE study separately, TPT desensitization was also observed (main effect of *Trial* $F_{2, 32} = 53.348$, $p < .001$, $\eta^2_p = 0.769$), but the exposure did not affected this desensitization.

Analysing the combined UMTS and LTE data only the between-trial desensitization effect was detected (main effect of *Trial* $F_{1.45,52.06} = 245.460$, $p < .001$, $\eta^2_p = 0.872$) without any effect of *Exposure*.

Results of the Stroop test

No main effect of *Exposure* was found in any condition (interference: $F_{1,48} = 1.038$, $p = 0.313$, $\eta^2_p = 0.021$; facilitation: $F_{1,48} = 0.000$, $p = 0.998$, $\eta^2_p = 0.000$), thus exposure had no effect on any Stroop test measures. N.B., the features of the Stroop test itself (such as the appearance of interference and facilitation) were demonstrated, which confirmed the reliability of our test. The colour naming task induced longer RT than word naming ($F_{1,48} = 41.608$, $p < .001$, $\eta^2_p = 0.464$) and the participants gave slower responses in the incongruent condition (interference: $F_{1,48} = 132.155$, $p < .001$, $\eta^2_p = 0.734$) and faster responses in the congruent condition (facilitation: $F_{1,48} = 34.116$, $p < .001$, $\eta^2_p = 0.415$) than in the neutral condition. The significant main effect of *Time* ($F_{1,48} = 36.289$, $p < .001$, $\eta^2_p = 0.435$) indicated an effect of practice.

Results of resting EEG mesasurements

Alpha power was significantly reduced in the real RF exposure compared to sham (main effect of *Exposure*: $F_{1,53} = 6.338$, $p = 0.015$, $\eta^2_p = 0.107$; see Figure 1.). An effect of *Exposure* was shown during (Mid) and after (Post) exposure blocks compared to the pre-exposure (Pre) period (*Exposure* effect in Mid and Post exposures relative to Pre period as baseline: $F_{1,53} = 6.475$, $p = 0.014$, $\eta^2_p = 0.109$). The effect did not differ between Mid and Post exposure periods (*Exposure* × *Time* Mid vs. Post: $F_{1,53} = 2.202$, $p = 0.144$, $\eta^2_p = 0.040$).

The analysis (with baseline correction) was also performed separately for the UMTS and LTE experiments. The results were similar: LTE exposure significantly reduced EEG alpha power (LTE *Exposure* Mid and Post vs. baseline: $F_{1,20} = 5.095$, $p = 0.035$, $\eta^2_p = 0.203$) while a similar (marginally significant) effect was found for the UMTS exposure (UMTS *Exposure* Mid and Post vs. baseline: $F_{1,33} = 3.772$, $p = 0.061$, $\eta^2_p = 0.103$). In accordance with the above, the analysis of the pooled data of the two RF types (UMTS and LTE) showed no significant main effect of ($F_{1.53} = 0.724$, $p = 0.399$, $\eta^2_p = 0.013$) or interaction with the *RF type* as a between-subject factor.

The mass univariate analysis also yielded concordant results. In the data pooled across RF types, a significant *Exposure* effect was found ($p_{Cluster} = 0.005$). The topographic distribution of the difference covered the whole scalp in the mid- and post-exposure period (with only very subtle apparent differences between them), but with no difference in the pre-exposure period. UMTS and LTE data analysed separately resulted in marginally significant differences with this method as well (UMTS: $p_{Cluster} = 0.067$, LTE: $p_{Cluster} = 0.055$), whereas testing for an *RF type* × *Exposure* interaction yielded no suprathreshold clusters.

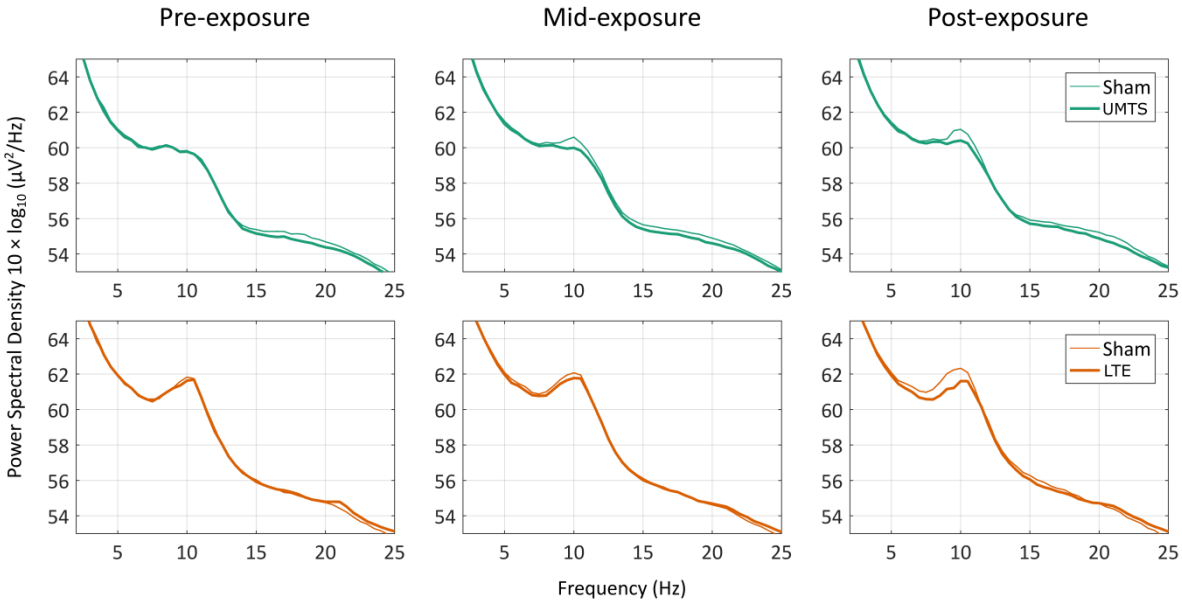

Figure 1.: EEG spectral power density of real (UMTS and LTE) and Sham sessions before (Pre), during (Mid) and after (Post) exposure, averaged for all EEG electrodes.

Summary

Due to the extremely rapid spread of mobile communication technology, various health issues have been raised in the field of non-ionizing radiation. Due to the general use of MPs, RF exposure levels of the population have also significantly increased; also, MPs are mostly used directly next to the head, which thus absorbs a significant ration of the RF power. So far, research initiatives have been focusing on the effects of previously used mobile telecommunication system generations (e.g., GSM), so it has been of particular importance to examine the potential adverse effects of RF radiation generated by the new signal generations (UMTS, LTE) MPs on the central nervous system.

Here we investigated whether acute RF radiation emitted by UMTS and LTE exposure systems causes any (potentially adverse) alteration in pain-related responses measured in he TPT or in cognitive brain functions reflected by the Stroop-effects and the strength of alpha band EEG oscillations.

The paradigm for TPT measurement was successfully validated in a capsaicin-induced hyperalgesia model clearly demonstrating that the device sensitively measures capsaicin-induced acute hyperalgesia. In the RF EMF exposure experiments, we found that while acute UMTS exposure had a short desensitizing effect on the TPT on the hand contralateral to the exposure side, the LTE exposure did not cause such effects. The volunteers' subjective

reporting on the perceived pain intensity (based on the visual analogue scale assessment) was in agreement with the TPT results. Changes in TPT may have occurred due to the reducing effect of RF on objective pain discrimination, which was manifested in a decrease in sensitization by repeated stimulation. The fact that only one type of RF (UMTS) caused change in pain perception thresholds suggests that the different effects may have been caused by the difference in the physical parameters (e.g., the signal modulation) between the two types of RF radiation (UMTS vs. LTE).

None of the RF types had any effects on cognitive performance measured in the Stroop test. At the same time, both UMTS and LTE exposure reduced the amplitude of EEG oscillations in the alpha band. Decreased alpha activity due to RF exposure may indicate an acute effect on oscillatory neurodynamics, which may potentially interfere with attentional processes through a change in the temporal coordination of information processing. However, in our case the effect in alpha activity reflecting network-level modifications was not followed by changes in higher-order cognitive performance (processing speed, selective attention, etc.). This is presumably due to the low exposure power or the acutely induced compensatory processes of the healthy brain.

In order to reach a more complete conclusion on possible physiological and/or adverse effects of the newer RF telecommunication technologies, more studies are needed with similar rigorous design and experimentation to find out whether RF EMF exposure with other radiation parameters (frequency, modulation and absorbed performance) alters the information processing of the healthy brain.

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ICNIRP. 2018b. Guidelines on Limiting Exposure to Time-Varying Electric, Magnetic and Electromagnetic Fields (100 kHz to 300 GHz) Appendix B: Health Risk Assessment Literature.

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Publications

Publications related to the thesis

1. **Vecsei Z**, Csatho A, Thuroczy G, Hernadi I. 2013. Effect of a single 30 min UMTS mobile phone-like exposure on the thermal pain threshold of young healthy volunteers. Bioelectromagnetics 34:530-41. **IF: 1.859**

2. **Vecsei Z**, Thuróczy G, Hernádi I. 2018. The Effect of a Single 30-Min Long Term Evolution Mobile Phone-Like Exposure on Thermal Pain Threshold of Young Healthy Volunteers. International Journal of Environmental Research and Public Health 15:1849. **IF: 2.145**

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Posters related to the thesis

1. **Vecsei Z**, Csathó Á, Thuróczy G, Hernádi I (2010). The effects of 30 min 3G mobile phone exposure on thermal pain threshold in healthy human volunteers. IBRO International Workshop 2010. Pécs, Hungary, January 21-23. (poster presentation, abstract)

2. **Vecsei Z**, Csathó Á, Bakos J, Thuróczy G, Hernádi I (2011). No effects of 30 min UMTS mobile phone exposure on thermal pain threshold in young healthy human volunteers, EBEA International Conference 2011. Rome, Italy, February 21-24. (poster presentation, abstract)

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1. Kőszegi Zs, Kállai V, Atlasz T, Babai N, Kovács P, **Vecsei Z**, Wilhelm M, Hernádi I (2007). Compound 48/80 hatása a thalamikus hízósejtekre normál ivari ciklusú, és ovariectomizált nőstény patkányokban. XI. MITT konferencia 2007. Szeged, Hungary, January 24-27. (poster presentation, abstract)

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