Do GSM 900MHz signals affect cerebral blood circulation? A near-infrared spectrophotometry study

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Abstract: Effects of GSM 900MHz signals (EMF) typical for a handheld mobile phone on the cerebral blood circulation were investigated using near-infrared spectrophotometry (NIRS) in a three armed (12W/kg, 1.2W/kg, sham), double blind, randomized crossover trial in 16 healthy volunteers. During exposure we observed borderline significant short term responses of oxyhemoglobin and deoxyhemoglobin concentration, which correspond to a decrease of cerebral blood flow and volume and were smaller than regular physiological changes. Due to the relatively high number of statistical tests, these responses may be spurious and require further studies. There was no detectable dose-response relation or long term response within 20min. The detection limit was a fraction of the regular physiological changes elicited by functional activation. Compared to previous studies using PET, NIRS provides a much higher time resolution, which allowed investigating the short term effects efficiently, non-invasively, without the use of radioactive tracers and with high sensitivity.

OCIS Codes: (170.1470) Blood/tissue constituent monitoring

References and links

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1. Introduction

Recent studies have shown that pulsed high-frequency electromagnetic fields (EMF) affect human sleep and sleep electroencephalogram (EEG) [1, 2]. Effects on regional cerebral blood flow (CBF) and weak effects on the heart rate were observed [3-6]. Positron emission tomography (PET) was used to record regional blood flow [3, 5, 6]. In studies [3, 5, 6] subjects were exposed 30min to radiofrequency (RF) EMF having the same signal scheme as

a global system for mobile communications (GSM) phone at 900MHz. The first PET scan was taken 10 min after the end of exposure. In [6] the subjects were assessed by PET during the exposure to EMF. In all studies increases as well as decreases in CBF were found, but the decreases seemed more prominent during exposure. PET achieves a three-dimensional spatial resolution of approximately 5mm and can measure CBF and cerebral blood volume (CBV). Its time resolution is very low, i. e. in the range of ~min, since each measurement requires a separate injection of a radioactive tracer. PET is therefore suited to measure long-lasting effects, but unable to detect immediate changes in CBF and CBV. The previous findings [3, 5] encourage further investigations with a higher time resolution for detecting potential changes and to use a method allowing the assessment of immediate responses in CBF and CBV to electromagnetic radiation.

In this study near-infrared spectrophotometry (NIRS) with a data acquisition rate of 100Hz is used. This technique has been well established as a tool to study activity of the brain [7-9] and e.g. applied to record changes in oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) concentrations in the visual and motor cortices during functional stimulation (e.g.[10]). Simultaneous comparison measurements of NIRS to fMRI [11] and PET [12] showed good agreement. O_2Hb and HHb are closely related to CBF and CBV. NIRS is highly sensitive to changes in O_2Hb and HHb and is able to measure changes in the hemoglobin concentration in the order of per mills [13]. In addition NIRS is non-invasive, painless, relatively inexpensive, uses non-ionizing radiation, measures continuously and can be repeated as often as necessary.

The main aim of the study was to assess with a higher time resolution than in previous studies changes in O_2Hb or/and HHb in response to EMF using a protocol similar to functional studies. The different types of responses investigated include changes in O_2Hb or/and HHb during exposure (short term), between exposures (short term) and differences in trends between exposure and sham sessions over the entire experiment (long term). In addition a potential dose-response relation was assessed using two different exposure strengths differing by a factor of 10 in power. The results were compared to functional responses during regular brain activation.

2. Methods

2.1. Near-Infrared Spectrophotometry

The principle of NIRS is described extensively in [13, 14]. In short, a near-infrared light source is placed on the head. At a certain distance a detector measures the intensity of the light, which re-emerges from the tissue. It has been shown that the photons, which travel from the source to the detector carry information about the brain [11]. Thus from the changes in light intensity, information about the changes in the blood circulation of the brain can be obtained.

Tissue can be optically characterized by two parameters: scattering and absorption. Theoretical models for light transport through tissue have been derived, mainly by using the diffusion approximation to the Boltzmann transport equation for the semi-infinite boundary condition. Using this approximation, mathematical models have been derived and tested to analyze the optical data and quantify O_2Hb and HHb concentration changes [14-16]. These algorithms are now well established.

For the detection of changes in CBF and CBV, it is sufficient to quantify changes in O_2Hb- and HHb- concentration. The sum of O_2Hb and HHb equals to the total hemoglobin concentration (tHb), which is proportional to the CBV and can be used to calculate the CBV. A change in CBV leads to a parallel change in both O_2Hb and HHb [10]. In contrast a change in CBF leads to a parallel change in O_2Hb and an opposite change in HHb [10]. In the rest of this paper we will consider the primary NIRS parameters O_2Hb and HHb.

For imaging applications a mesh of sources and detectors is placed on the region of interest. The measured data provides spatially resolved O_2Hb- and HHb- concentrations.

For this study the High Speed Optical Brain Imager MCP II, developed in our laboratory and described in [13] was used. The instrument is equipped with light emitting diodes (LEDs)

for two wavelengths at 730nm and 830nm. It provides a data acquisition rate of 100Hz and a resolution of 16bit. Two imaging sensors allow covering an area of twice 2.5cm x 3.75cm with 16 channels each and produce 2D images of the changes in O_2Hb and HHb.

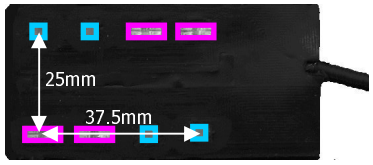

Fig. 1. The configuration of the sensor. Purple quadrangles indicate source positions with LEDs and blue squares indicate PIN photodiode detectors.

A trigger signal can be directly read through an analog input. This was used to record the EMF on and off status during the experiment.

2.2. Exposure System

The same exposure system as in [2-4] was used. The exposure system has been extensively characterized including the dosimetry, e.g. the dose within different head tissues dependent on the input power of the antenna [4]. The same pulse-modulated, "handset-like" GSM signal (900MHz carrier) as in [2-4] at two different power levels (average pulse peak power of 12 and 1.2W/kg spatial peak specific absorption rate (SAR) averaged over 10g of tissue) was applied. For the chosen exposure protocol this results in an averaged spatial peak SAR of 1.5W/kg for the highest power level over the course of the experiment. The study room was particularly suitable for these measurements, because it provided a constant ambient temperature and silence. Ambient magnetic fields measured by a Wandel & Goltermann EM Filed Analyzer EFA3 between 5Hz and 30kHz were 53.4±5.2nT and thus neglectable.

2.3. Electromagnetic interference

In a test prior to this study the exposure system generating a defined SAR distribution in the head was operated together with the NIRS instrument to warrant electromagnetic compatibility of all the equipment involved. The NIRS equipment was mounted on an experimental phantom used for compliance testing of mobile phones filled with tissue simulating liquid. This phantom also had similar optical properties as the human head and thus was appropriate to assess the influence of EMF on the NIRS measurement and vice versa. The antenna used for exciting the EMF was positioned according to the experimental setup.

The signal of the NIRS instrument was recorded for different positions of the sensor at the head, including the ones used below, during on/off cycles of the radiation from the antenna. The EMF lead to electromagnetic interference (EMI) on the NIRS signal, which increased linearly proportional to the power of the EMF. The size of the interference was also dependent on the location. However, the effects on the NIRS-signals were synchronous to the EMI, i.e. they disappeared immediately once the EMF was turned off. To obtain NIRS-signals without the influence of EMI, the protocol provides intermittent periods without EMF.

For the same configurations with and without NIRS equipment the distribution of the SAR was measured and compared. The influence of the sensor on the SAR distribution in the head can be significant depending on the orientation of the connecting cable. Therefore, by using an appropriate positioning of the cable these effects can be reduced. The sensor causes slightly higher maximum spatial peak SAR values in the head. However, this deviation is <0.5dB for our configurations and is well below the limits required by current safety guidelines.

These steps ensured the safety of the volunteers participating within the studies and the correct function of all equipment involved.

2.4. Study protocol

Our protocol was derived from a standard protocol to study changes in the blood circulation associated with functional activation of the brain [8]. Neuronal activity increases the oxygen consumption, which in turn leads to an increase in blood flow to provide more oxygen. The increase in blood flow overcompensates for the consumed oxygen, resulting in a net oxygenation increase in the activated area, i.e. an O_2Hb increase and a HHb decrease. Blood flow changes may also occur spontaneously. To clearly identify changes associated with brain activity, a study protocol usually includes at least ten periods, where stimulation and rest are alternated. By averaging these periods all spontaneous changes not related to stimulation are removed. Since it takes approximately 10s for the blood flow change to fully develop, stimulation or rest periods >10s are usually applied.

Based on the previously found effects of EMF on cerebral blood flow, we defined the following four hypotheses that were to be tested by our study:

1. There is a short term response of O_2Hb or/and HHb to EMF within 20s during exposure.
2. There is a short term response of O_2Hb or/and HHb to EMF within 40s after exposure.
3. There is a long term response of O_2Hb or/and HHb to EMF, which occurs within 20min.
4. There is a dose-response relation, i.e. the change in O_2Hb or/and HHb is higher:
   a. When exposed to a higher EMF dose.
   b. When comparing the two sides of the head, one towards, one opposite to the antenna.

The study was designed as a three armed, double blind, randomized crossover trial. Each subject underwent three exposures (spatial peak SAR 12W/kg, 1.2W/kg, sham exposure) in randomized order on three different days, making measurements at the same time of day for each subject. Randomization was achieved by computer. All displays, which would indicate the type of exposure, were covered for the whole period of measurement, such that neither the operator nor the subject had any indication of the type of exposure. Thus, a double blind measurement environment was secured.

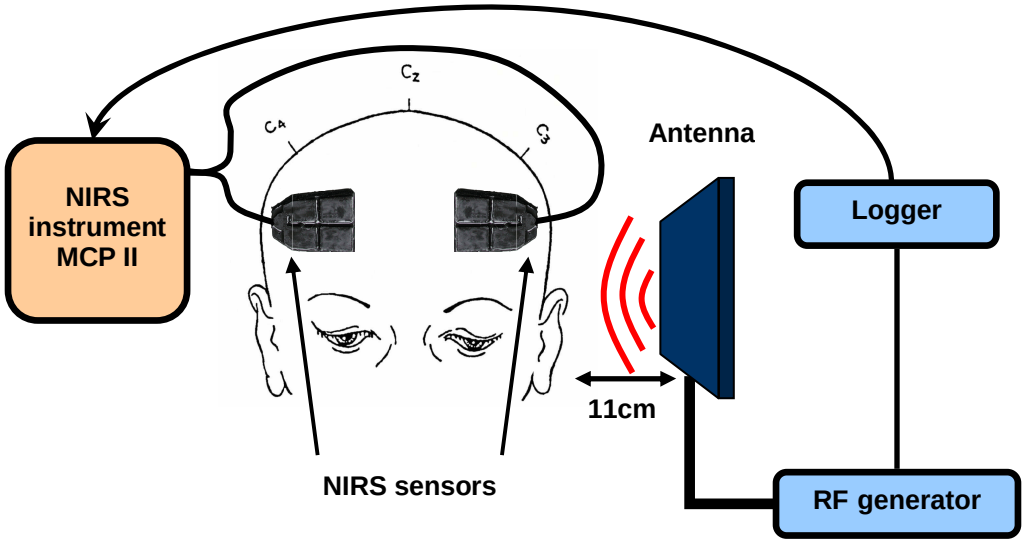

Fig. 2. Diagram of the experimental set-up. The sensors were placed above area B (MNI coordinates: x=-56, y=10, z=20) on the left hemisphere and the respective position on the other hemisphere

The subjects were asked to refrain from caffeine, nicotine, and cell phone use for 2 hours prior to the measurement. Prior to the measurements we obtained the following information from the subjects: age, handedness, sleep quality, tiredness, and degree of consumption of

caffeine, nicotine and cell phone use. We also noted room and outside temperatures. During the experiment subjects were seated on a chair, asked to remain completely still and to count backwards from 2000 in order to keep the prefrontal cortex in steady activity. The antenna was positioned on a location close to the left ear, typical for a handheld mobile phone (Fig. 2). One NIRS-sensor was placed on area B of the prefrontal cortex identified in a PET-study, where an increase in CBF was measured [3]. The other sensor was placed on the same area at the right hemisphere.

In a pilot study we found that shortly after placing the sensors on the head, the O_2Hb and HHb concentration changed. Possible reasons for this are described in detail in the discussion section. Since the strongest changes occur within the first two minutes, we introduced a 4 minute baseline measurement prior to the main trial period. The baseline period allowed parameters to settle after the initial changes. The trial period consisted of 15 repeated cycles, which included 20s exposure (2s on / 2s off, alternating) and 60 second rest. The 2s on / 2s off cycles were established to provide periods free of EMI within each measurement. The whole duration of a measurement was 24min.

After each measurement subjects communicated what number they had reached in counting backwards and guessed, whether he/she was exposed to radiation or not.

This study was approved by the Ethical Committee of the County of Zurich.

2.5. Subjects

18 healthy volunteers were enrolled in this study. The subjects received a reimbursement for their participation and gave written informed consent prior to the measurements.

2.6. Data analysis

The logarithm of the intensity data was taken and each light bundle was divided by the interoptode distance and a differential pathlength factor of 6.48 for 730nm and 5.82 for 830nm. The 2s on periods during exposure were detected and excluded from the analysis. Since during exposure periods, every other interval of 2s was missing, every other period of 2s was excluded also for the rest of the measurement. The data were averaged over periods of 2s. The mean and standard deviation of periods of 20s, i.e. five of these 2s intervals, were calculated.

Movement artifacts were detected and removed in the following way: If the standard deviation of a 20s period exceeded 2.5% of the mean, a movement artifact was assumed to be present. The respective period was rejected. A particular cycle thus consists of four periods of 20s, one before exposure (*Pre*), one during exposure (*Exp*), one directly after exposure (*Post1*) and one beginning 20s after exposure (*Post2*). If one period of 20s was rejected within a particular cycle the other three periods were rejected as well. The same is true for data at the other wavelength within a particular path.

From the remaining intensity data, concentration changes in O_2Hb and HHb were calculated according to standard procedures [14]. The *Pre* period was subtracted from the *Exp*, *Post1*, *Post2* and following Pre periods to obtain changes due to exposure. A time triggered average was calculated for each subject and for each light path. For the assessment of short term effects (during exposure to up to 40s after exposure) we considered the Exp, Post1 and Post2 periods. For the assessment of long term effects the average difference between successive Pre periods was multiplied by the number of repetitions (15) to obtain the concentration change during the 20min of measurement. Since no localized changes within the sensor were discernible, all locations with the same interoptode distance were averaged for each subject.

The statistical analysis was carried out separately for the data of each interoptode distance. The differences between three exposures (12W/kg, 1.2W/kg, sham exposure) were analyzed by analysis of variance for each of the differences between Pre and the other periods. A difference was assumed to be statistically significant for $p \leq 0.05$. Furthermore, each combination of two types of exposure was compared by a nonparametric paired Wilcoxon test. Due to multiple testing (Bonferroni) a difference was assumed to be statistically

significant for a reduced $p \leq 0.016$. The variances between the three types of exposure were compared using a Levene's test.

To estimate the limit of detection, i.e. the size of the change we would have been able to detect, we first calculated the difference between the three exposure types for each parameter and distance and checked for normality of the distribution. Finally we calculated the 95% confidence interval (CI 95%) for these differences and averaged the values across the period of Exp, Post1 and Post2.

3. Results

3.1. Subjects

The data of two subjects were rejected due to too many movement artifacts. The remaining 16 subjects had a mean age of 31.2±6.3 (SD). 15 subjects were male and 14 right handed.

Between the different exposure types there was no significant difference for sleep quality, tiredness, caffeine or nicotine consumption, cell phone use, outside temperature, and inside temperature. Also the speed of the counting did not depend on the exposure type. Subjects were not able to guess, whether they were exposed to EMF or not, i.e. there was no significant correlation between the guess of the subjects and the true situation. This also can be seen as an indication for intact blinding.

3.2. Short term changes in O2Hb and HHb

The short term changes in O_2Hb and HHb concentration during the three types of exposure are displayed in Fig. 3 to Fig. 6. There were a few significantly different means or variances between exposure types for the short term effects, which are identified in the captions and discussed below.

3.3. Long term changes in O2Hb and HHb

The long term changes in O_2Hb and HHb concentration during the three types of exposure are displayed in Fig. 7. There were no significant differences between the three exposure types.

3.4. Detection limit

The CI 95% is an indicator of the detection limit of the current study. To estimate the size of effects that could have been detected, the CI 95% of the difference between the three exposure types was calculated and averaged. It was ±0.052µM (1.25cm distance), ±0.086µM (2.5cm) and ±0.138µM (3.75cm) for HHb and ±0.120µM (1.25cm distance), ±0.147µM (2.5cm) and ±0.198µM (3.75cm) for O_2Hb.

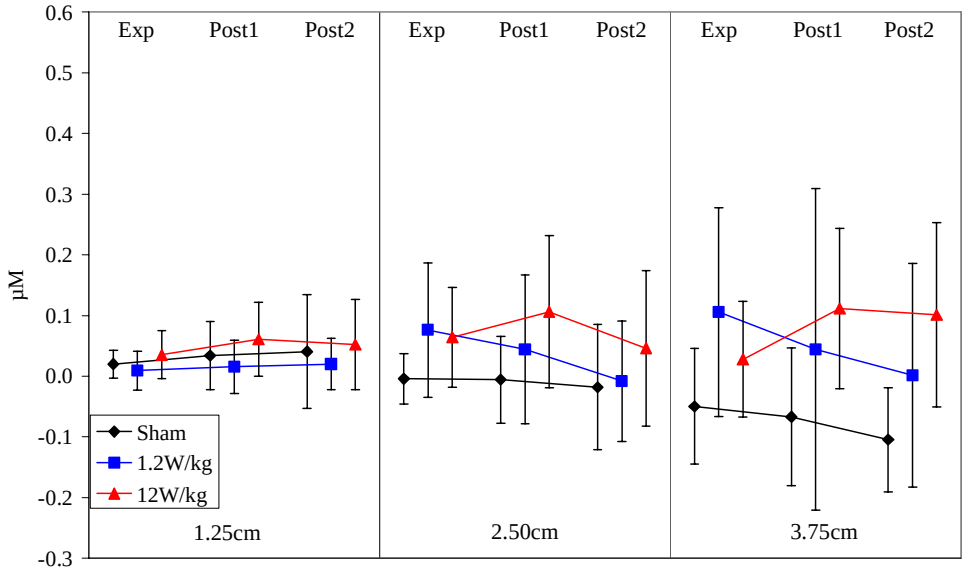

Fig. 3. The short term changes in deoxyhemoglobin (HHb) concentration during three types of exposure: 12W/kg, 1.2W/kg and sham. Data were obtained from the left side of the head, which was towards the antenna. The symbols indicate the mean and the whiskers the 95% confidence interval (CI 95%). The results are displayed separately for the three different interoptode distances of 1.25cm (left), 2.5cm (middle) and 3.75cm (right). The depth of the interrogated tissue depends on the interoptode distance, i.e. the short distance of 1.25 mostly detects changes in the superficial layer of the head (skin and skull), while the longest distance also contains information about the brain. The data are displayed for the different periods of measurement: the 20s of exposure (Exp), the first 20s after exposure (Post1) and the second 20s after exposure (Post2). At 1.25cm the difference between HHb during exposure with 12W/kg and 1.2W/kg is statistically significant ($p=0.011$, Wilcoxon). Furthermore, the CI 95% between sham and 1.2W/kg was significantly different at 2.5cm distance for the Exp ($p=0.001$) and Post1 ($p=0.015$) periods. Otherwise there were no significant differences between the three types of exposure.

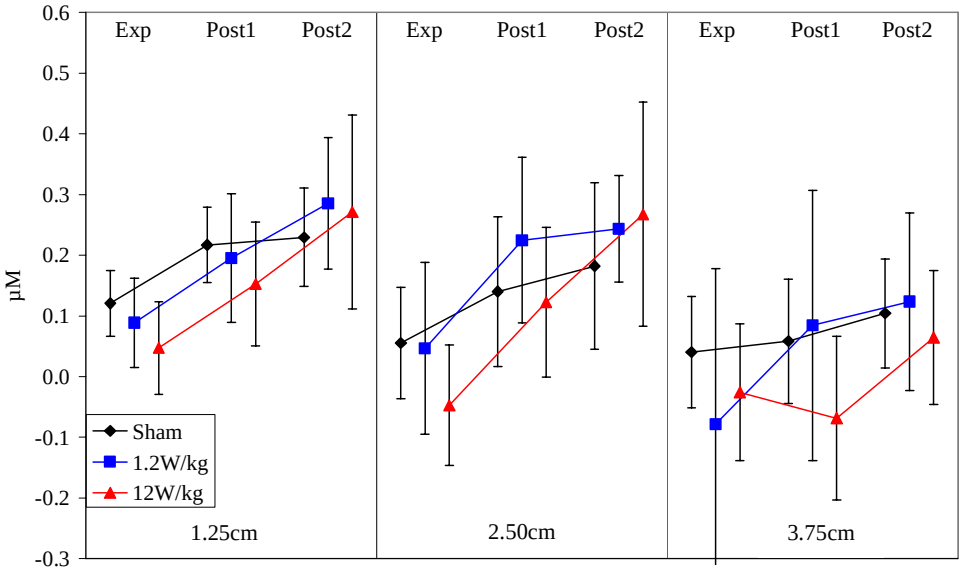

Fig. 4. The short term changes in oxyhemoglobin (O_2Hb) concentration during three types of exposure: 12W/kg, 1.2W/kg and sham. Data were obtained from the left side of the head, which was towards the antenna. This figure is analogous to Fig. 3. At 2.5cm the difference between O_2Hb during exposure with 12W/kg and sham is statistically significant (p=0.016, Wilcoxon). Otherwise there were no significant differences between the three types of exposure.

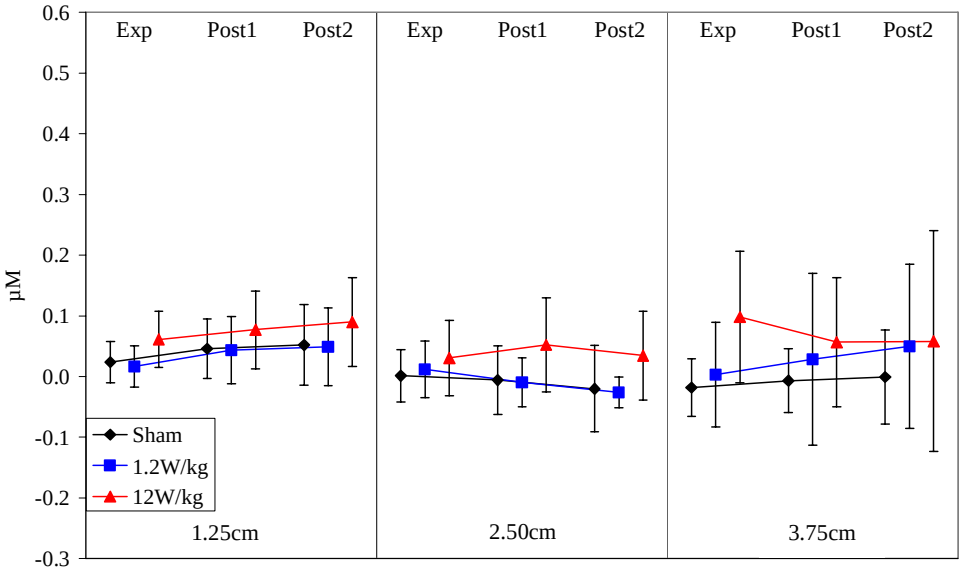

Fig. 5. The short term changes in deoxyhemoglobin (HHb) concentration during three types of exposure: 12W/kg, 1.2W/kg and sham. Data were obtained from the right side of the head, which was on the opposite side of the antenna. This figure is analogous to Fig. 3. The CI 95% between sham and 12W/kg was significantly different at 3.75cm distance for the Post1 (p=0.011) period. There were no other significant differences between the three types of exposure.

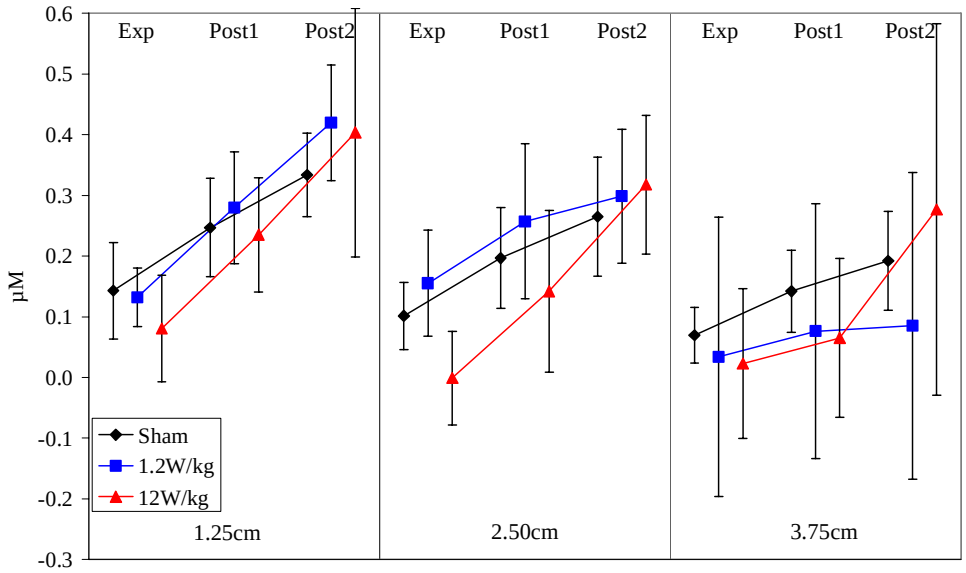

Fig. 6. The short term changes in oxyhemoglobin (O_2Hb) concentration during three types of exposure: 12W/kg, 1.2W/kg and sham. Data were obtained from the right side of the head, which was on the opposite side of the antenna. This figure is analogous to Fig. 3. At 2.5cm the difference between O_2Hb during exposure with 12W/kg and 1.2W/kg is statistically significant (p=0.009, Wilcoxon) and analysis of variance showed a significant difference between the three types of exposure during this period (p=0.009). Otherwise there were no significant differences between the three types of exposure.

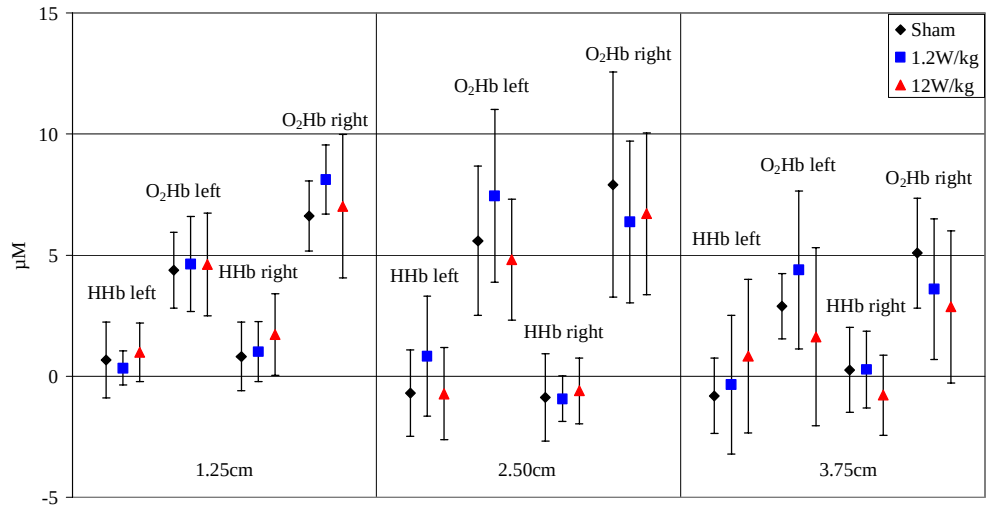

Fig. 7. The long term changes over 20min in oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) concentration during three types of exposure: 12W/kg, 1.2W/kg and sham. The results are displayed separately for the three different interoptode distances of 1.25cm (left), 2.5cm (middle) and 3.75cm (right). The data from the left side was close to the antenna while the right side was further away form the antenna. The whiskers correspond to the CI 95%. There were no significant differences between the three exposure types.

4. Discussion

4.1. General consideration about NIRS data

The current study applies one specific signal at 900MHz using a defined temporal pattern to study a potential alteration in blood circulation. The protocol of this study was similar to the ones used for studying functional activity of the brain. In principle several types of NIRS methods could have been used for this study. CBF can be assessed using a tracer, diffusing-wave spectroscopy (DWS) and standard NIRS. As tracers O_2 [17, 18] and indocyanine green [19, 20] have been used. O_2 is only feasible as a tracer in mechanically ventilated subjects, while an injection of indocyanine green could also be applied to study a healthy population. As all methods using a tracer, the time resolution is low (~min), because every measurement requires an injection of the tracer, which is the reason why we did not employ this method. DWS is a method based on the analysis of variation in the speckle interference patterns. The amount of variation depends on the blood flow in tissue. Although DWS [21, 22] is a sensitive method with a high time resolution, which could in principle also image CBF, the interpretation of the dynamic data depends on the optical parameters of tissue. In addition to obtain information on the CBV and oxygenation a separate NIRS system needs to be added. In the future DWS may become the tool of choice, however, at the moment we preferred to apply the more established standard NIRS technique, which is also highly sensitive, has a high time resolution and images changes in O_2Hb and HHb concentration. From these changes in CBF and CBV can be derived with standard NIRS as outlined above and the algorithms are quite well established. The standard NIRS system including the sensor geometry used in this study was specifically built for functional studies.

NIR light has a limited penetration depth, which depends on the interoptode distance, for 1.25cm the mean penetration depth is approximately 5mm and for 3.75cm it is 9mm. However, photons travel much deeper, information from the brain activity at a depth of 2.5cm was previously detected [11]. Currently work is in progress to resolve different layers of tissue. Noise increases with interoptode distance. The optimal distance is a tradeoff between sensitivity to deep layers of tissue and signal to noise ratio. Therefore, typically for studies of functional activity a distance of 2.5 to 3.0cm is used.

For the interpretation of the data, it is helpful to keep in mind the regular changes of blood circulation of the brain as assessed by functional NIRS or other regular physiological processes. The peak magnitude of the changes in O_2Hb and HHb functional activity in the motor cortex assessed with our instrument corresponds to approximately 0.85µM or 0.25µM, respectively, which is in agreement with other published data [10, 23-25]. In the visual cortex usually higher magnitudes of 2.5µM for O_2Hb and 0.6µM for HHb were found [10, 26, 27].

Another regular physiological process is the change in O_2Hb and HHb concentration due to slow vasomotion. This occurs at a rate 1/10s. The magnitude of these changes is in the order of 1µM for O_2Hb and 0.2µM for HHb [26].

The regular cerebral tHb concentration corresponds to approximately 73.8±15.0µM [28].

4.2. Long term changes in O_2Hb and HHb

As Fig. 7 displays, there is a considerable drift of approximately 5µM for O_2Hb and 1µM for HHb during the long term measurement. It is also clearly visible that this drift is larger for short interoptode distances. Thus this drift is related to a superficial effect. In addition the pattern of this drift, an increase in O_2Hb and small changes for HHb indicates an increase in superficial blood flow. There are several reasons, which could lead to such an effect. E.g. the area where the sensor is attached to the head is insulated from the ambient air. This may lead to an increased temperature and thus an increased local blood flow. Another possible effect could be the pressure exerted by the sensor due to the elastic bandage, which fixates it. This pressure leads to a lower blood flow immediately after the beginning of the application of the sensor. An increase in blood flow could be initiated by physiological effects to counteract the initial decrease in blood flow or by a slight decrease in pressure exerted by the elastic bandage over time, which would again lead to an increase in blood flow. The drift of the NIRS

instrument is 0.005µM/min and therefore cannot account for this effect. Due to our randomized crossover design of the trial, the drift affects all three exposure types in each subject in the same way, which effectively prevents errors.

Whatever the origin of the effect leading to this drift is, there were no significant differences in the drift between the different types of exposure. Thus, there were no long term effects of exposure visible.

4.3. Short term changes in O_2Hb and HHb

The long term drift is overlayed to the short term effects displayed in Fig. 3 to Fig. 6. Keep in mind that this drift is usually eliminated by a detrending operation in publications describing functional brain activity. We did not detrend the data to avoid any spurious effects.

We found the following three significant short term concentration changes: On the left exposed side of the head at 1.25cm (Fig. 3), the difference between HHb concentration during exposure with 12W/kg and 1.2W/kg was statistically significant (p=0.011, Wilcoxon, reduced significance level of 0.016 due to Bonferroni). On the left exposed side of the head at 2.5cm (Fig. 4) the difference between O_2Hb during exposure with 12W/kg and sham is just statistically significant (p=0.016, Wilcoxon). On the right side of the head, which was on the opposite side of the antenna (Fig. 6), at 2.5cm the difference between O_2Hb during exposure with 12W/kg and 1.2W/kg is statistically significant (p=0.009, Wilcoxon) and analysis of variance showed a significant difference between the three types of exposure during this period (p=0.009).

For the CI 95% there were again three significant differences between exposure types. On the left exposed side of the head for HHb at 2.5cm (Fig. 3), the CI 95% was significantly different between 12W/kg and 1.2W/kg for the EXP (p=0.001) and Post1 (p=0.015) periods (Fig. 3). On the right side of the head, at 3.75cm for O_2Hb the CI 95% was significantly different (p=0.011) between 12W/kg and 1.2W/kg for the Post1 period (Fig. 5).

Otherwise there were no significant differences between the three types of exposure.

How can these statistically significant differences be interpreted? The p-value gives the likelihood of a statistical type I error, i.e. the probability to detect a difference by chance, when in reality there is none. Multiple testing increases the risk of obtaining significant differences by pure chance, e.g. for 20 tests we will detect one statistically significant (p=0.05) difference just by chance. For the analysis of variance, we carried out 36 tests (3 exposure types x 3 distances x 2 sides x 2 substances). Thus we expect approximately two significant differences just by chance. The same likelihood applies for CI 95% and the paired Wilcoxon test. Since none of the detected significance levels is high, we conclude that there is a high probability that the detected significances are due to chance.

Keeping this in mind let us consider, what the physiological meaning of the significant differences would be, if they were real. The general pattern of the differences is a decrease in O_2Hb and a smaller increase in HHb with exposure to EMF. This indicates a decrease in blood flow and blood volume. Thus, a thermal short term effect of EMF can be excluded, because it would lead to an increase in blood flow and volume. Since most of the significant differences were found at a distance of 2.5cm, they are unlikely to originate from superficial layers of tissue (see also below).

The significant increase in HHb on the exposed hemisphere at 1.25cm distance is very small (0.026µM), i.e. five times smaller than the response to functional activity. It is noteworthy that it is the difference between 1.2Wkg exposure and 12W/kg exposure and that the difference to sham is not significant.

The significant decrease in O_2Hb on the exposed hemisphere at 2.5cm distance is also very small (0.102µM), i.e. eight times smaller than the response to functional activity. This difference occurs between sham and 12W/kg exposure.

The significant decrease in O_2Hb on the opposite hemisphere of the exposure at 2.5cm distance is also small (0.156µM), i.e. six times smaller than the response to functional activity. Again it is noteworthy that it is the difference between 1.2Wkg exposure and 12W/kg exposure and that the difference to sham is not significant. Unless we postulate that a low

dose leads to the opposite effect of a higher dose of EMF, this pattern seems to be unlikely. Furthermore, the dose of EMF on the opposite hemisphere was approximately eight times lower than on the exposed side. It is difficult to explain, why an effect on the opposite side of the exposure should be larger than on the exposed side.

Thus in conclusion, in the unlikely case that the effects found were true, they would be between 5.4 to 9.6 times smaller than the effects due to functional activation and they would indicate a decrease in blood flow and volume, which corresponds to the effects of a deactivation of the brain [29].

4.4. Detection limit

The difference between the three exposure types that could have been detected compared to changes associated with regular functional activity, is approximately five times (1.25cm distance), three times (2.5cm) and twice (3.75cm) lower for HHb and seven times (1.25cm distance), six times (2.5cm) and four times (3.75cm) lower for O_2Hb. Thus, we can exclude that the change due to exposure with EMF exceeds these limits. This also means that, if there was a change in blood circulation due to EMF, it would certainly be smaller than the regular physiological changes.

The detection limit increases with the distance, because the noise level increases with distance. The significant changes in O_2Hb observed at a distance of 2.5cm originate from deeper layers of tissue, because at 1.25cm no significant change was observed even though at such a distance a superficial change would have been detected with a higher statistical power.

In principle the detection limit depends on the noise level of the different components of the measurement: the instrumental noise including shot noise, the physiological noise and the noise due to movement artifacts. According to the previously published [13] values the instrumental noise for our set-up is below 0.001µM. Thus the main sources of noise in our measurements were the physiological noise and the noise due to movement artifacts.

In conclusion the low noise level of our measurements allows detecting changes in blood circulation, which are one seventh to one half of the regular physiological changes in blood circulation.

4.5. Limitations and strengths of NIRS

NIRS is mostly sensitive to capillaries [30], which is an advantage compared to other methods such as PET or MRI, because it is more sensitive to local effects.

The current instrument is sensitive to EMI, because there are electronic devices in the sensor. The interferences could be eliminated by using fiber optics. This would enable to analyze potential effects at a higher time resolution (e.g. 100Hz). In addition this would enable to remove some of the physiological noise caused by the heart beat and thus increase the signal to noise ratio.

Short term effects have to the best of our knowledge not been studied so far.

In previous studies the modulation of the signal has been identified as a relevant factor for long term effects. Correlations between on/off cycles and effects are not yet clear. Studies using the same exposure system and pulse-modulated GSM signals but PET instead of NIRS [3, 5] detected changes in blood flow. These studies differed by the following factors: The timing and power of the GSM signals was different, i.e. our signals were only applied intermittently and at an accordingly higher power within the time slots. Our NIRS-measurements were continuous, which required a longer attention span of the subjects and limited the assessment of the long term effects to 20min instead of 30min during the PET study. The influence of these factors on the signals detected with PET is unknown and therefore our long term results are not contradicting the ones found in the mentioned PET studies.

In the latest PET study [6], a decrease in CBF was found beneath the antenna, which may seem to confirm our results. However, the set-up used in this study was considerably different from our set-up concerning the exposure system, the task and the timing.

5. Conclusions

Borderline significant immediate responses of O_2Hb and HHb to EMF were found, i.e. within 20s during exposure. These responses correspond to a decrease of CBF and CBV. They were much smaller than regular physiological changes in O_2Hb and HHb elicited e.g. by functional activation of the brain. As discussed above there is a high probability that these responses are due to chance. Therefore, these effects require further studies.

There was no detectable response of O_2Hb or/and HHb to EMF within 40s after exposure. There was no detectable dose-response relation. No lateral differences have been found. The detection limit was a fraction of the regular physiological changes elicited by functional activation. There was no detectable slow response of O_2Hb or/and HHb to EMF, which occurs within 20min.

Compared to previous studies using PET, NIRS provides a much higher time resolution, which allowed investigating the existence of immediate effects efficiently, non-invasively, without the use of radioactive tracers and with high sensitivity.

Acknowledgements

We gratefully acknowledge the funding for this research project by the Research Foundation Mobile Communication at the Swiss Federal Institute of Technology in Zurich (ETHZ) and by the Federal Office of Public Health, which also supported the pilot study as well as the extension of the main study. We thank Dr. Derek Brown, Dr. Jürgen Schuderer, Sven Ebert and Dr. Walter Oesch for their technical support and assistance. We also would like to thank PD Dr. Peter Achermann, Dr. Mirjana Moser and Prof. Niels Kuster for valuable advice and all the subjects for their participation.