Whole Brain EEG Synchronization Likelihood Modulated by Long Term Evolution Electromagnetic Fields Exposure

Bin Lv, *IEEE Member*, Chang Su, Lei Yang, Yi Xie, and Tongning Wu, *IEEE Member*

***Abstract*— In this paper, we aimed to investigate the possible interactions between human brain and radiofrequency electromagnetic fields (EMF) with electroencephalogram (EEG) technique. Unlike the previous studies which mainly focused on EMF effect on local brain activities, we attempted to evaluate whether the EMF emitted from Long Term Evolution (LTE) devices can modulate the functional connectivity of brain electrical activities. Ten subjects were recruited to participate in a crossover, double-blind exposure experiment which included two sessions (real and sham exposure). In each session, LTE EMF exposure (power on or off) lasted for 30 min and the EEG signals were collected with 32 channels throughout the experiment. Then we applied the synchronization likelihood method to quantify the neural synchronization over the whole brain in different frequency bands and in different EEG record periods. Our results illustrated that the short-term LTE EMF exposure would modulate the synchronization patterns of EEG activation across the whole brain.**

I. Introduction

During the past few years, many neurophysiological and neuroimage studies have been applied to investigate whether radio frequency electromagnetic fields (EMF) produced by mobile phone have an influence on human brain [1]. Compared with other tools, Electroencephalography (EEG) has better compatibility with the exposure system and therefore becomes the most widely used approach in this area [1]. During these studies, EMF exposure environment was setup by the real mobile phone or other experimental device. EEG signals were then recorded to characterize the brain activities and used to evaluate the possible modulation caused by EMF exposure.

From the perspective of EEG data analysis, most previous studies divided EEG signals into different frequency bands and compared their power spectrum among different exposure conditions. For example, resting EEG studies have consistently reported Global System for Mobile Communications (GSM) EMF exposure enhanced the alpha activity in midline posterior sites [2] and other brain regions [3, 4]. It is well known that human brain is a complex organization which simultaneously satisfies two basic principles, that is, functional segregation of specialized neural information processing in distinct brain regions and functional integration of some regions into networks [5]. Thus, it is necessary to investigate whether EMF exposure would modulate the functional connectivity among different brain regions. Vecchio et al used event-related coherence (ERCoh) method to estimate the coherence variation of homotopic EEG channels among different exposure conditions, and found that GSM EMF from mobile phone affected the interhemispheric synchronization of temporal and frontal resting EEG rhythms in normal young [6] and elderly subjects [7]. However, till now, no study investigated the EMF influence on functional connectivity across the whole brain.

Besides coherence analysis, there have been lots of measures to characterize EEG synchronization based on different underlying assumptions. They can be categorized into bivariate or multivariate, linear or nonlinear, model based or data-driven, and so on (see more discussion in [8, 9]). Among them, synchronization likelihood was proposed based on the detection of simultaneously occurring patterns along the neural signals [10]. It is a robust multivariate nonlinear estimator which has be widely used to estimate the pattern of statistical interdependencies between two or more EEG signals during cognitive task [11] and the possible alternation in patients with some brain diseases [12].

In this paper, we present our recent work about EMF effect on brain functional connectivity with synchronization likelihood method. We designed a controllable Long Term Evolution (LTE) EMF exposure environment at 2.573 GHz, and recruited ten healthy subjects to participate in the exposure experiment. EEG signals were recorded in different exposure conditions. Synchronization likelihood was used to identify the functional coupling between each pair of EEG channels. In the end, we performed statistical analysis to evaluate whether the whole brain patterns of synchronization likelihood were modulated by the acute LTE-related EMF exposure.

II. Methods

A. Experiment Setup

In order to avoid the subjective bias or any other influences, we designed a double-blind, crossover, randomized and counterbalanced exposure study. The exposure setup was similar to our previous studies [13, 14]. In brief, the exposure source was simulated by a dipole antenna (SPEAG AG, Zurich, Switzerland) which was placed on the right ear with 1 cm distance, and the LTE exposure signal at 2.573 GHz was produced by a CMW 500 (R&S, Munich, Germany) and an RF amplifier (AR, Bothell, WA, USA). For each subject, there were two sessions including real exposure (power on) and sham exposure (power off). Both sessions

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were performed with an interval of one week. In each session, the exposure lasted 30 min, and there were 10 min for rest before and after the exposure. Therefore, each session included three periods (Pre-Expo, During-Expo and Post-Expo).

B. EEG Data Acquisition

Ten healthy subjects (all males, and mean age: 25.2±4.4 years) were recruited in this study. Written informed consent was obtained from all subjects after the experimental procedure had been fully explained. During the experiment, subjects were instructed to sit on the chair with their eyes closed and minimize the movement. EEG signals were recorded from 32 channels which were covered the whole brain according to International 10-20 system (NT9200 digital EEG system, Symtop Instruments, Beijing, China). For each subject, we collected about two 50 min (10 min Pre-Expo + 30 min During-Expo + 10 min Post-Expo) EEG data. The sampling frequency was 1000 Hz.

C. EEG Data Pre-processing

EEG data pre-processing was performed by using toolbox EEGLab [15]. First, we performed the visual inspection for artifact rejection. The EEG signals were then segmented into 2 sec epochs and any epochs with voltage exceeding ±150 μV were rejected for further analysis. In order to improve the computational efficiency, the raw data were down-sampled from 1000 Hz to 250 Hz. Independent component analysis (ICA) decomposition was used to eliminate the contributions of some obvious artifact sources, such as head movement, eye blinks, muscle activities and so on [15]. Finally, the artifact-corrected data were filtered to generate the signals in four frequency bands of interest which were defined as [16]: theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz) and broadband (4-30 Hz).

D. Synchronization Likelihood Calculation

Synchronization likelihood is an unbiased generalized synchronization measure which can be used to detect linear and nonlinear interdependencies between pairs of time series [10]. Assume two EEG signals x_i, y_i $(i = 1 \ldots N)$, where i represents discrete time. We applied time-delay embedding method to construct time delay vectors X_i and Y_i in state space. Synchronization likelihood takes into account the chance that if the distance between X_i and X_j is very small, the distance between Y_i and Y_j will also be small. Therefore, synchronization likelihood between x and y at time i is defined as follows [8, 10]:

$$SL_i = \frac{1}{2(w_2 - w_1 - 1)p_{ref}} \sum_{\substack{j=1 \\ w_1 < |j-i| < w_2}}^{N} \theta(\varepsilon_{x,j} - |X_i - X_j|)\theta(\varepsilon_{y,j} - |Y_i - Y_j|) \quad (1)$$

Here, $|\cdot|$ is the Euclidean distance and θ is the Heaviside step function (that is, $\theta(x) = 1\ if\ x > 0, otherwise\ \theta(x) = 0$). w_1 and w_2 are two windows, w_1 is the Theiler correction for autocorrelation effects, w_2 is a window that sharpens the time resolution of the synchronization measure and they are chosen such that $w_1 \ll w_2 \ll N$. $\varepsilon_{x,j}$ and $\varepsilon_{y,j}$ are the critical distances which are determined by probability $p_{ref} \ll 1$. Thus, the intermediate coupling is reflected by $p_{ref} < SL_i < 1$ [8, 10].

We can get the synchronization likelihood values for given time periods by averaging SL_i for all time i $(i = 1 \ldots N)$. In the present study, we used the following parameters for SL_i computation: embedding dimension = 3, time delay = 78 samples, $w_1 = 78$ samples, $w_2 = 204$ samples, $p_{ref} = 0.05$.

We calculated the synchronization likelihood values between all pairs of EEG channels in four frequency bands of interest (theta, alpha, beta and broadband) and six EEG record periods (Pre-Expo, During-Expo and Post-Expo in real/sham exposure). In this way, we obtained twenty-four symmetric 32 x 32 functional connectivity matrices for each subject. Different matrices represented the synchronization likelihood values for channel combination in different frequency bands and record periods.

The summary of the experimental paradigm and data processing pipeline was shown in figure 1. Synchronization likelihood calculation was carried out by using toolbox HERMES [9].

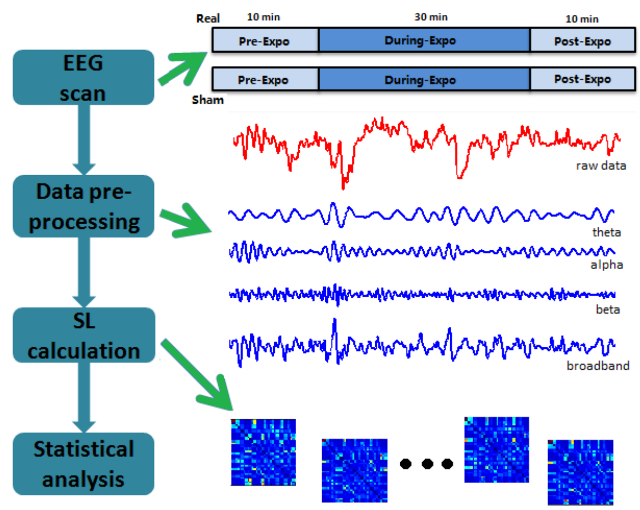

Figure 1. Schematic diagram of the experimental paradigm and data processing pipeline. EEG signals were recorded during real exposure and sham exposure. Each exposure session included three conditions: 10 min Pre-Expo, 30 min During-Expo and 10 min Post-Expo. After artifact correction, the raw EEG data (red line) were filtered to yield signals in four defined frequncy bands (blue lines). Synchronization likelihood was calculated for each pair of EEG channels in different frequency bands and different exposure conditions. Twenty-four functional connectivity matrices were genertated for each subject. Finally, statistical analysis was performed to detect their differences throughout the conditions of EMF exposure.

E. Statistical Analysis

In order to evaluate the possible changes of synchronization likelihood values in different conditions of LTE EMF exposure, we obtained the relative synchronization likelihood by subtracting the values of Pre-Expo period from periods of During-Expo and Post-Expo. This calculation was similar to the previous definition of EEG ERCoh [6, 7]. Then we applied random-effects paired t tests to compare the relative synchronization likelihood between real and sham exposure. All statistical results were corrected for multiple comparisons with false discovery rate (FDR) method at a significant level of $p < 0.05$.

III. RESULTS

Figure 2 showed the results for During-Expo period by using paired t tests. We could find that, compared with sham exposure, LTE EMF exposure modulated the pattern of synchronization likelihood in different frequency bands. In theta band, most of statistical differences appeared in the right hemisphere (Fp2<->Fc4, T4<->Tp8, T4<->T6, T6<->Pg2, C4<->Pg2 and Cp4<->Pg2). In alpha band, the statistical differences of functional coupling were mostly linked from channel Cz and Oz. And channel Fz became the main junction channel for statistical differences in beta band. When frequency range was selected from 4 to 30 Hz, there were four functional coupling showing statistical differences (T4<->Tp8, T4<->T6, Fz<->Cp3 and F7<->Ft7).

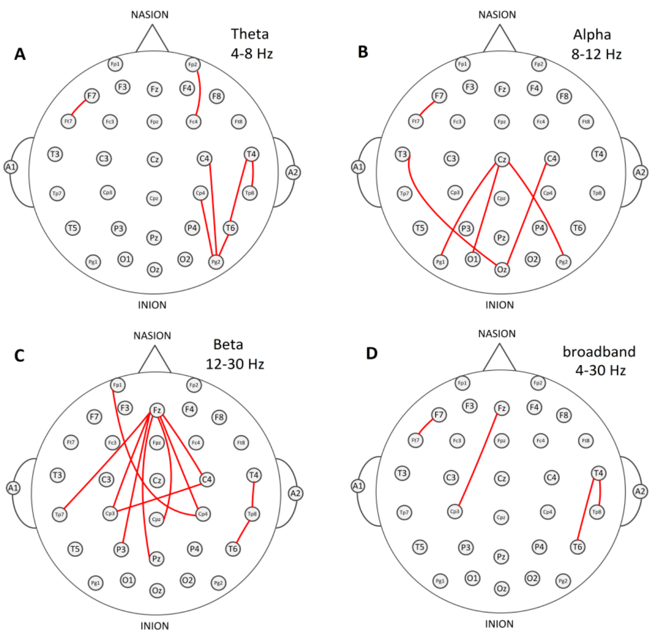

Figure 2. The statistical differences of relative synchronization likelihood for During-Expo between real and sham exposure.The black cycles represent the EEG channel positions over the scalp (A1/A2 are the ground electrodes in left/right ear). And the red lines represent the places where the staitistical differences of relative synchronization likelihood exist between the corresponding EEG channels ($p < 0.05$, FDR corrected). (A) is the result in theta band (4-8 Hz); (B) is for alpha band (8-12 Hz); (C) is for beta band (12-30 Hz); and (D) is for broadband (4-30 Hz).

Figure 3 showed the detected statistical differences for Post-Expo period between real and sham exposure. We observed the patterns of synchronization likelihood were modulated after LTE EMF exposure. There were different patterns within different frequency bands. And they were not the same as that in During-Expo period. Most of statistical differences were located in the frontal and central lobes. In particular for broadband (4-30 Hz), the statistical differences of functional coupling appeared in left prefrontal areas (F7<->Tp7 and Ft7<->C3) and middle prefrontal areas (Fp1<->Fp2, Fp1<->F4, Fp2<->F4, Fc3<->Fpz, Fc4<->Fpz and Fz<->Fpz).

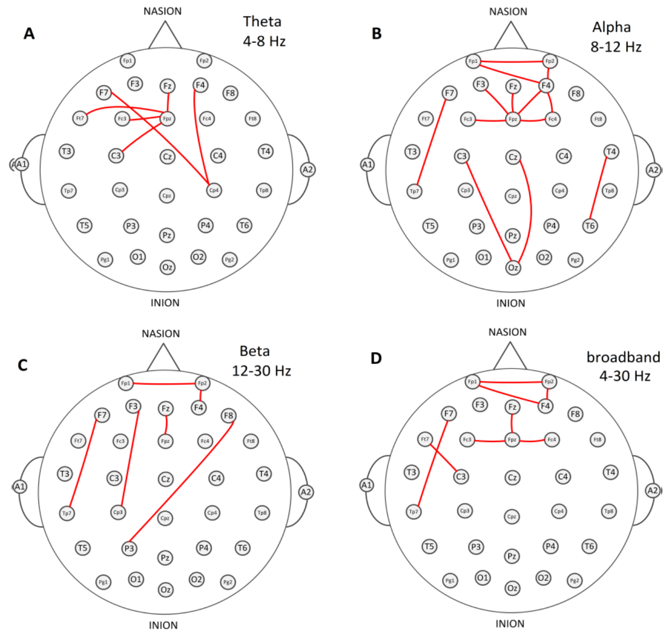

Figure 3. The statistical differences of relative synchronization likelihood for Post-Expo between real and sham exposure ($p < 0.05$, FDR corrected). The diagrammatic representations (including black cycles and red lines) are the same as figure 2. (A) is the result in theta band (4-8 Hz); (B) is for alpha band (8-12 Hz); (C) is for beta band (12-30 Hz); and (D) is for broadband (4-30 Hz).

IV. CONCLUSION AND FUTURE WORK

In this study, we used EEG technique to investigate the possible effect on brain activities caused by the short-term LTE EMF exposure. The synchronization likelihood method was applied to quantify the neural synchronization of EEG signals during and after LTE EMF exposure. The analysis was performed over the whole brain in four frequency bands of interest. The results provided us some evidences that the short-term LTE EMF exposure would modulate the synchronization patterns of EEG activation across the whole brain.

In our previous work, we have applied the resting state functional magnetic resonance imaging (fMRI) technique to examine the change of spontaneous brain activities induced by LTE EMF exposure [14]. After the real exposure, we found that the decreased amplitude of low frequency fluctuation in some brain regions which mostly located in medial frontal gyrus, left and right temporal gyrus [14]. Due to the compatibility with exposure system, EEG signals could be simultaneously examined during the EMF exposure. Therefore, this present study investigated the pattern of synchronization likelihood not only after exposure (figure 3, Post-Expo period) but also during exposure (figure 2, During-Expo period). The place of statistical differences were mostly located in left prefrontal areas (theta band, alpha band, broadband in During-Expo period, and all frequency bands in Post-Expo period), middle prefrontal areas (beta band in During-Expo period, and all frequency bands in Post-Expo period), and right temporal areas (theta band, beta band, broadband in During-Expo period, and alpha band in Post-Expo period). The exposure site was near the right side of ear. Therefore, the above results demonstrated that LTE EMF exposure modulated the synchronization patterns of brain activation not only in the closer brain areas but also in the remote areas and even in the contralateral brain area. This phenomenon was similar to our previous finding with fMRI [14] and many other studies [17, 18].

In the future, we can segment EEG signals into smaller time epochs and estimate the synchronization likelihood in each time epoch. And then, we can also apply graph theory [19, 20] to evaluate the dynamic changes of synchronization pattern in different EMF exposure conditions.

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