Coupling functions between brain waves: Significance of opened/closed eyes

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ABSTRACT

In dynamical systems, the information flows converge or diverges in state space and is integrated or communicated between different cells assemblies termed as CFC. This process allows different oscillatory systems to communicate in accurate time, control and distribute the information flows in cell assemblies. The CF interactions allow the oscillatory rhythms to communicate in accurate time, and reintegrate the separated information. The intrinsic brain dynamics in Electroencephalography (EEG) with eye - closed (EC) and eye open (EO) during resting states have been investigated to see the changes in brain complexity i.e. simple visual processing which are associated with increase in global dimension complexity. In order to study these changes in EEG, we have computed the coupling to see the inhibitory interneurons response and inter-regions functional connectivity differences between the eye conditions. We have investigated the fluctuations in EEG activities in low (delta, theta) and high (alpha) frequency brain oscillations. Coupling strength was estimated using Dynamic Bayesian inference approach which can effectively detect the phase connectivity subject to the noise within a network of time varying coupled phase oscillators. Using this approach, we have seen that delta-alpha and theta-alpha CFC are more dominant in resting state EEG and applicable to multivariate network oscillator. It shows that alpha phase was dominated by low frequency oscillations i.e. delta and theta. These different CFC help us to investigate complex neuronal brain dynamics at large scale networks. We observed the local interactions at high frequencies and global interactions at low frequencies. The alpha oscillations are generated from both posterior and anterior origins whereas the delta oscillations found at posterior regions.

Keywords: Electroencephalography (EEG) during resting state, Cross Frequency Coupling, Dynamic Bayesian Inference, Wavelet Transform

1. INTRODUCTION

dynamics in EEG over different frequencies bands. [2] reported different cross frequencies coupling relations such as amplitude to amplitude, phase to phase and phase to amplitude at different frequencies. [3] observed that oscillatory activates in human and animals modulated in various frequency bands and found that fast gamma oscillation (30-150 Hz) is modulated by the slow theta oscillation (5-8 Hz). The intracranial electrical recordings measured in human such as EEG, EMG are reflected by the oscillatory electrophysiological signals. The theta and beta both bands are modulated during memory and perception tasks. [4] reported that during neuronal delta phase (1-4 Hz) have modulated the theta amplitude (4-10 Hz) and theta phase has modulated gamma (30-50 Hz) amplitude thereby controlling the baseline excitability through oscillatory hierarchy resulting stimulus related response in the neuronal ensemble. These studies have been reported in monkeys that theta phase and gamma power interactions are found in auditory cortex during both stimulus driven activity and auditory cortex. A theta-gamma interaction in continuous word recognition memory task in human medical temporal lobe was observed by [5]. A robust high and low frequency bands coupling in the human brain ongoing electrical activity was observed by [6] which disseminate the activity in cortical area showing effective mechanism for communication during cognitive process in human. The studies also reveal that cross – frequency coupling where the frequency band of one oscillation modulates the activity in different frequency bands are ampler in animal than in human. [7] [8][9] reported that spike timing of single neuron and firing rate can be modulated by theta rhythm and intracortical local field potential by the gamma power as reported by [4] [7] [10]. Moreover [11] [12] [13] observed the changes in theta powers during task related activities in the human. [14] have detected the cross-frequency coupling at frequencies up to 40 Hz at scalp. [1] also reported that classical power spectral analysis based on Fast Fourier Transform (FFT) or different time- frequency transforms (e.g. Hilbert, Wavelet, or Gabor transform) unable to identify the relationships among different frequencies or frequency component as merely because these techniques are based on amplitude modulation with a set of defined frequencies across time whereas complex transformation in the complex signals like EEG, EMG containing different frequency components interacting with each other require a corresponding complex transformation of the signal to provide information about the phase changes. Thus cross-frequency coupling (CFC) technique is hypothesized between different frequency bands which serves as local as well as global interaction among the processes and related directly to the integrated distributed information.

Cross-frequency coupling (CFC) can be investigated using different approaches i.e. using PSI for phase-amplitude coupling as described by [18] and correlation coefficients between different frequency components i.e. phase-phase CFC (or n:m phase synchronization) as described by [15] [17] [20]. [20] used first time the n:m phase synchronization technique based on phase synchronization of chaotic oscillator to evaluate the temporal evolution of the coordinated peripheral tremor activity affected directly by the time course of strength of synchronization in neural network involving cortical motor areas.

To observe the evolution of natural processes in time and space scientists have used the systematic observations to analyze the nature. The physiological systems are highly complex in nature. The complexity of physiological and behavioral control systems decreases with aging and disease. Thus, loss of complexity (require analysis from methods of nonlinear dynamics) is due to the loss or impairments of functional components and or altered non-linear coupling functions (require time-frequency coherence and cross frequency coupling methods). Hussain et al used complexity based methods [53] [54] [55] [63] to investigate the dynamics of nonlinear dynamics of physiological time series. They observed that structural components loss with respect to pathological conditions. Rathore [57] [58] [59] extracted geometric and hybrid features to detect and investigate the dynamics of Colon Cancer. Hussain et al used Machine learning [61] [62] for heart rate variability classification and face detection, neural networks [64] for emotion recognition, [60] support vector machine for load forecasting and [57] time-frequency spatial wavelet phase coherence to investigate the dynamics in EEG during resting state. Typically, every one aimed to generate models based on collected data over specified time interval and its dependency that how the faster processes be whether seconds or milliseconds. To analyze the data, different methods of data analysis be employed as suggested by [20] [22] [23] [24] [32] depending on the characteristic of data may be for example Bayesian methods, particle filters, Kalan filters, maximum likelihood estimators etc. The Bayesian methods are preferably used to detect the dynamics in the systems not isolated but may be influenced by environment and other weekly coupled processes [25] [27]. Recently, [20] [28] used the Bayesian method to identify the time-varying dynamics even in presence of noise because of its ability to detect the dynamics in presence of noise and follow the time evolution of the parameters. The dynamical Bayesian inference method can be applied to various types of dynamical systems including coupled oscillatory dynamical systems e.g. neuronal systems or cardio-respiratory [1] [19] [29] which are time varying dynamical systems subject to external noise. The method can also be applied for detecting causal interactions, directionality of influence [1] [30] [31], synchronization and coherence [15] [21] [33] [34] and coupling functions [23] [32] [35]. We here aimed to detect the cross-frequency coupling and coherence between Eye-closed and open subjects during resting states at 19 electrodes according to 10-20 international system. Dynamical Bayesian inference method) already used by [36] to investigate the cardiorespiratory coupling functions affected by aging.

2. METHODS

Coupling Function

To understand the interaction between two unidirectional coupled oscillators, consider an example of two coupled oscillators [35] with phases φ_1, φ_2.

$$\begin{aligned}\dot{\varphi}_1 &= \omega_1 + f_1(\varphi_1, \varphi_2) + \xi_1 \\ \dot{\varphi}_2 &= \omega_2 + f_2(\varphi_1, \varphi_2) + \xi_2 \quad (1)\end{aligned}$$

Where $\omega_{1,2}$ are the autonomous, natural frequencies of first and second oscillators and f_2 is a coupling function added to the frequency of second oscillator. This coupling function will influence the natural frequency of second oscillator depending on its magnitude values either accelerating or decelerating the second oscillator. The physics literature reveals this coupling as interaction between oscillators whereas the biology literature describes it as correlation between them e.g. due to phase locking (Pikovsky et al., 1997).

Using Hilbert transform, we obtained protophases ϑ are transformed to true phases φ [37] which grows uniformly in time. We aimed to check the functional influence of delta-alpha, alpha-gamma and theta-gamma waves for each case i.e. which wave influence and dominate the other wave. The delta waves are deep sleep in adult and waking in young adults and gamma waves are associated with attention, memory and sensory processing. Keeping the property of phase-dynamics [21[35] we can build the system of stochastic differential equation.

$$\begin{aligned}\dot{\varphi}_\alpha &= \omega_\alpha + f_\alpha(\varphi_\delta, \varphi_\alpha) + \xi_\alpha \\ \dot{\varphi}_\gamma &= \omega_\gamma + f_\gamma(\varphi_\alpha, \varphi_\gamma) + \xi_\gamma \\ \dot{\varphi}_\gamma &= \omega_\gamma + f_\gamma(\varphi_\theta, \varphi_\gamma) + \xi_\gamma \qquad (2)\end{aligned}$$

Where $\omega_{\alpha,\gamma}$ are the frequencies of oscillators, $f_{\alpha,\gamma}$, coupling functions, $\varphi_{\delta,\alpha,\theta,\gamma}$ represents the corresponding angles and $\xi_{\alpha,\gamma}$ represents the stochastic part modelled as white and Gaussian noise where the natural frequency is affected by the coupling influence of each corresponding oscillator.

The differential equation 2) can be decomposed into Fourier components as [47].

$$\dot{\varphi}_i = \sum_{k=-K}^{K} c_k^{(i)} \varphi_{i,k}(\varphi_i, \varphi_j) + \sqrt{N}\xi_i \qquad (3)$$

Dynamical Bayesian Inference

The cross-frequency coupling from phase oscillators is to be inferred from Bayesian approach [20, 21]. Consider a time series $X = \{x_m = x(t_m)\}\ (t_m = mh)$, where m=1,2,3,…..,M. from which phase dynamics are extracted (Luchinsky et a., 2008; 73]. Using Dynamic Bayesian inference, we aimed to compute a set of model parameters $M = \{c_k^{(i)}, N_{r,s}\}$ where $c_k^{(i)}$ denote the coupling and $N_{r,s}$ denote the noise matrix. Thus using Bayes' theorem, we can infer the unknown model parameter M from X by calculating posterior density $p_X(M|X)$, given a prior density $p_{prior}(M)$ that encompass the previous knowledge of unknown parameters based on observations and likelihood function $l(X|M)$ i.e. the conditional probability density to observe X given choice of unknown dynamical model M:

$$p_X(M|X) = \frac{l(X|M)\ p_{prior}(M)}{\int l(X|M)\ p_{prior}(M)dM} \qquad (4)$$

For high sampling frequency, i.e. small sampling step h, the phase dynamics in eq. 1can be well approximated using Euler midpoint discretization as:

$$\varphi_{i,m}^{*} = (\varphi_{i,m} + \varphi_{i,m+1})/2 \; and \; \varphi_{\cdot,m}^{*} = (\varphi_{i,m+1} - \varphi_{i,m})/h.$$
$$\varphi_{i,m+1} = \varphi_{i,m} + h\,\Psi\left(\varphi_{i,,m}^{*}, \varphi_{j,m}^{*}\middle| c\right) + h\sqrt{N}\, z_m \qquad (5)$$

Where z_m is the stochastic integral of the noise term over time i.e.

$$z_m \equiv \int_{t_m}^{t_{m+1}} Z(t)dt = \sqrt{h}\, H\, \xi_m$$

Here H is the Cholesky decomposition of noise matrix N and ξ_m is normally distributed random variable vector. The joint probability density of z_m is employed to compute the joint probability density of process in respect of $\varphi_i(m+1) - \varphi_i(m)$ by imposing $P[\varphi_i(m+1)] = \det\left(J_{\xi}^{\varphi}\right) P(\xi)$, where $J_{\xi}^{\varphi}$is the Jacobin term of transformed variables calculated from base function $\varphi_{i,k}$.

Thus, the negative log-likelihood function $S = -\ln(X|M)\ is\ then\ express\ as$:

$$S = \frac{M}{2}\ln|N| + \frac{h}{2}\sum_{m=0}^{M-1} c_k \frac{\partial \Psi_k(\varphi.,m)}{\partial \varphi} + [\dot{\varphi}_m - c_k \Psi_k(\varphi_{\cdot,m}^{*})]^T (N^{-1})\left[\dot{\varphi}_m - c_k \Psi_k(\varphi_{\cdot,m}^{*})\right]) \qquad (6)$$

By considering prior probability of parameter M as multivariate normal distribution, and considering the quadratic form of log-likelihood (6), thus posterior probability will also be multivariate normal distribution. Thus, parameter c with particular distribution with mean $\overline{c}$ and covariance matrix$\sum_{prior} \equiv \epsilon_{prior}^{-1}$, the stationary point S can be recursively computed using the below equations:

$$N = \frac{h}{M}(\dot{\varphi}_m - c_k \Psi_k(\varphi_{\cdot,m}^{*}))^T \left(\dot{\varphi}_m - c_k \Psi_k(\varphi_{\cdot,m}^{*})\right),$$
$$r_w = (\epsilon_{prior})kw c_w + h\Psi_k(\varphi_{\cdot,m}^{*})(N^{-1})\dot{\varphi}_m - \frac{h}{2}\frac{\partial \Psi_k(\varphi.,m)}{\partial \varphi},$$
$$\epsilon_{kn} = (\epsilon_{prior})kw + h\,\Psi_k(\varphi_{\cdot,m}^{*})(N^{-1})\Psi_w(\varphi_{\cdot,m}^{*}),$$
$$c_k = (\epsilon^{-1})kw\, r_w \qquad (7)$$

Quantification of Coupling

From Dynamic Bayesian inference, from inferred parameter c can be used to quantify certain characteristics of coupling function either by computing quantitative measures or comparing different coupling mechanisms

Coupling Strength

For evaluating phase-phase cross frequency coupling, one need to determine the coupling strength inferred from parameter c estimated using Bayesian dynamics inference. This coupling strength corresponds to the coupling amplitude extracted from phase dynamics of the time series. Here we aim to compute the cross-frequency coupling of delta-alpha, alpha-gamma, theta-gamma frequency bands from 16 subjects of EEG with eye closed and eye open during resting states for selected frontal electrodes Fp1 and Fp2. Mathematically, the coupling strength is computed using the Euclidean norm of inferred parameters that corresponds to Fourier components of the coupling to oscillator φ_i from combination of oscillators ρ i.e.

$$\left\|f_{i:\rho}\right\| = \sqrt{\sum_k \left(c_k^{(i:\rho)}\right)^2} \qquad (8)$$

For one oscillator, there are $2{\times}K\ elements$ and its coupling strength is indexed into c' part out of $c^{(i)}\ vector$, similarly two oscillators are composed of $2^2{\times}K^2\ elements$ and coupling strength is indexed into $c''^{(i)}$ part of vector and accordingly same happen for more than two oscillators

3. RESULTS

The phase synchronization (phase-phase CFC or amplitude – amplitude CFC) plays vital role in the functioning of brain in different ways. The regulations in the inter-area communication was extensively studied by [39] [40] [41] [42] [43] where cross location and same frequency phases are coupled between different brain areas. Likewise, same location and cross frequency coupling can be served as potential mechanism in regulating communication in different spatio-temporal scales. The phase-phase CFC were also investigated by [44] [45] that serves as physiological mechanism to link the activities occurring significantly at different rates e.g. in NREM sleep, the firing rate patterns correlations are observed during learning with a rate of six to seven times faster. [8] investigated that different frequencies interactions provide means to understand the complex neural dynamics in the frequency specific neural networks. The processes in the brain could be efficiently integrated with neuronal cell assemblies that are oscillating with different frequency synchronously. These phenomena can provide enhanced combinational opportunities to store the complex temporal patterns and to optimize the synaptic weights used in conjunction with relevant algorithms. [6] investigated that cross - frequency coupling in the present research plays a vital role in cognitive learning, neuronal computation and communication.

We have computed phase-phase CFC in lower and higher frequency bands for 19 electrodes. Figure 1 to 2 depict the CFC using lower frequency CFCs delta-alpha, delta-beta, theta- alpha and higher CFCs theta-beta, theta-gamma and alpha-gamma. The strongest CFC was observed between and within delta and alpha, delta and theta frequencies using both temporal and spatial scales. These different CFCs show that there are different neuronal interactions at work. In EC delta-alpha the highest coupling was obtained at C4 electrode, delta-alpha the strongest coupling was found in central regions i.e. C3, C4 and Cz and right parietal P8. Similarly, in delta-theta the strongest coupling was found at frontal Fp1 and Fp2 probes. Moreover, in theta-beta CFC during EC coupling was found stronger in parietal P7 and Pz and left temporal T7. In theta-gamma coupling during EC it was found stronger in Fp1 and O2 whereas in alpha-gamma it was found stronger in occipital are O1 and O2 during EC.

Likewise, during EO delta-alpha coupling was found stronger in Cz, in delta-theta CFC, it was found stronger in frontal probes such as F3, F4, Fz, F7 and F8 and right temporal probe T8. In theta-alpha coupling was found higher in O1, while in theta-beta it was found stronger in Fz and F8 whereas in theta-gamma this coupling was highest in T8 and O2 and in alpha-gamma the highest coupling was found in T7, T8 and O2.

The significance map in Figure 1 to 2 denotes the statistically significance p-values computed using paired t-test. The strongest significance was found in delta-alpha and theta-alpha CFC in most of the electrodes in each 19 chosen electrodes. In delta-alpha CFC the very significant results are obtained at electrode Cz, the electrodes F3, F7, Fp1, Fz, O1 and O2 also exhibit just significant results while other electrodes show no significant results. Thus, left frontal and occipital shows the significant results with EO>EC and central Cz also shows the highest significance. In theta-alpha CFC the statistically very significant results are obtained at electrodes F4 and T8 while the electrodes F3, F7, Fp1, O1, P4, Pz and P7 also showed only significant results ($p<0.05$). The electrodes C4, O2 and P8 show almost significant results. Thus, the left frontal, occipital, parietal regions and right frontal F4, temporal T8 and parietal P4 regions shows the significant results in theta-alpha CFC.

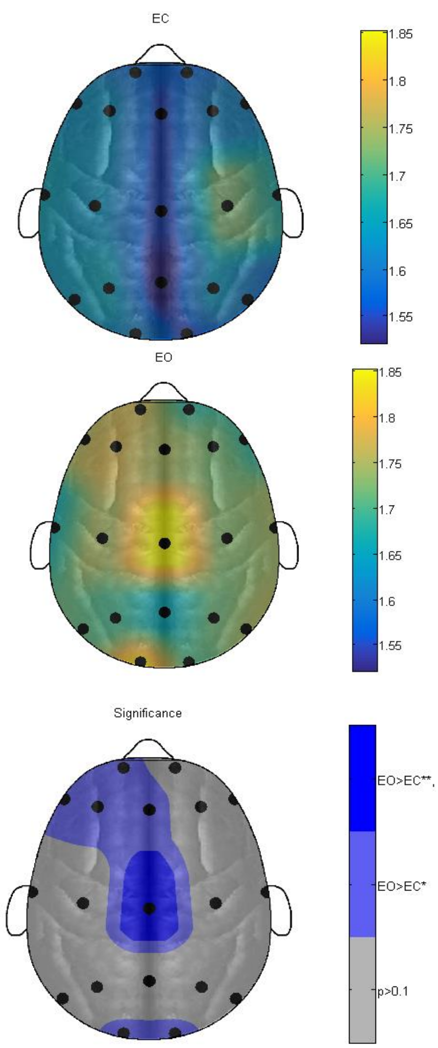

Figure 1: Delta-Alpha CFC EC, EO and Significance using paired test

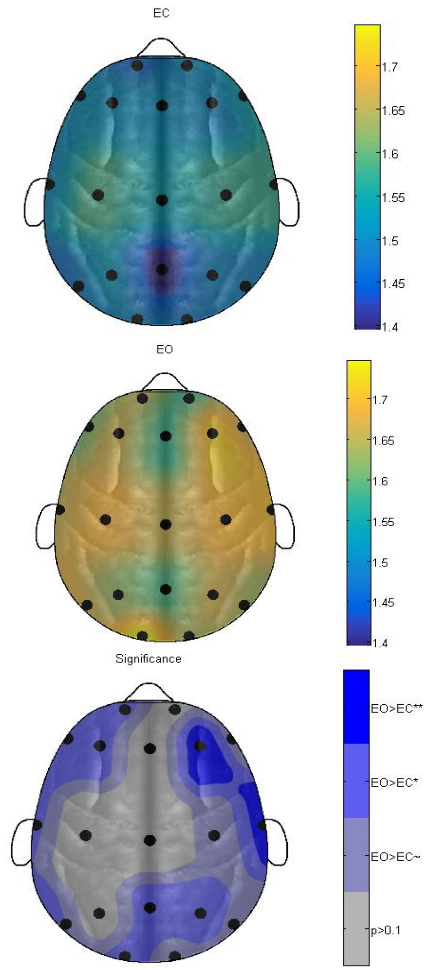

Figure 2: Theta-Alpha CFC EC, EO and Significance using paired test

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4. DISCUSSION AND CONCLUSION

In this study, we computed different discussed in below section:

Delta/theta-alpha CFC

Isleretal (2008) investigated the widespread CF phase coupling of delta-theta and delta-alpha rhythms where the delta oscillations phases are coupled to the localized theta and alpha oscillations in different regions central, posterior, right parietal regions etc. [1] in his study found that there exists delta-alpha (phase-phase and phase-amplitude) CFC in EEG resting state data. The coupling was seen within the parieto-occipital and frontal regions and these regions are connected via large scale couplings networks which show that there is a mechanism of direct communication in these regions in different cell assemblies. This coupling was found asymmetric from posterior-occipital to frontal regions especially during EC condition while during EO condition during rest this delta-alpha coupling can be found inverse.

Theta/Alpha-Gamma CFC

There are many theories that are describing the interplay between different frequency bands. They slow oscillations such as theta or alpha due to low frequency are considered to serve the network over long distances while the fast oscillations such as gamma due to high frequency are considered to synchronize the cell assemblies over short spatial scales [3]. [6] studied the theta/alpha-gamma and observed that phase-amplitude CFC vary across brain areas in different manners such as task-relevant manner and quickly changes in response to motor, sensory and cognitive events and also linked by the learning tasks performance. Moreover, this CFC was observed as distinct in brain rhythms, however it varies across function of task demands and cortical areas. For example, during auditory tasks, the theta-gamma CFC was higher than alpha-gamma at the anterior sites and equal across cortex, however, posterior alpha-gamma was observed greater than the anterior alpha-gamma CFC. Likewise, in visual tasks the alpha-gamma CFC was observed at posterior electrodes and found greater than theta-gamma CFC. Moreover, the theta-alpha phase detection coupling was recently studied in the frequency ranges (4-13 Hz) by [46] [47] [48].

At delta-alpha to alpha and theta-alpha to alpha CFC, the Coupling in EC condition is stronger in most cases than in EO condition and only few connections which are found stronger in EO than in EC. In delta-alpha to alpha CFC, stronger connection in EC are centro-occipital, temporo-central few parietal and frontal; in theta-alpha few stronger connections are found such as frontal, fronto-central, fronto-occipital, fronto-parietal, occipito-central. [1] also investigated CFC and found that in delta-alpha CFC showed large scale connections going from anterior to posterior where delta modulate alpha and using cross Bispectrum (cBIS) an inverse CFC modulation alpha to delta was observed. Where different delta-alpha or alpha-delta CFC directions are dependent upon the location of generation of delta and alpha generator. Previous studies [50, 51, 52] also revealed that alpha oscillations have posterior and anterior origins whereas delta oscillations have an anterior origin. Using both coupling directions and frequency generation origins, one might be able to investigate different types of CFC at a larger scale particularly when alpha oscillations are involved. Using coupling we also observed large scale coupling with alpha oscillation dominant from posterior to anterior direction which shows the influence of alpha frequency generator on other brain origins. This coupling was found large during EC may be due to inhibition as reported in the literature [49].

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