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Event Related Networks: On the Time-varying Small-World Topology of Functional Brain Networks

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Abstract. In recent years, different techniques have been used to study the topology of the functional brain networks. Nevertheless, only time-independent networks from long periods of brain activity have been reported. Here we propose a novel approach that allows to represent the evolution of the topologies in the time-frequency space: the *Event Related Networks* (ERN). Based in the traditional scheme used to study the event related potentials, the ERN framework allows to analyze the reconfigurations underwent by the brain networks as a response to external stimuli. Applied over a visual stimulus paradigm, it shows how the brain networks vary their functional connectivity in time and frequency, while maintaining their small-world structure. We consider that our approach provides a new methodology to elucidate the role of connectivity patterns over the ongoing brain dynamics.

Keywords: Brain Dynamics; Complex Networks; Functional Brain Networks; Small World Networks; Magnetoencephalography; Event-Related Fields.

1. Introduction

In recent years, the complex networks framework has provided increasingly challenging tools for the study of complex and collaborative phenomena [Boccaletti et al., 2006]. For the brain, both anatomical and functional networks have been found to exhibit small-world (SW) features. This specific topology is an interesting model for brain connectivity because on the one hand, for *anatomical connections*, SW topology allows to connect distant areas while maintaining an optimized wiring cost. For *functional connections*, it assures an efficient transfer of information by integrating local and global processes, while being capable of adapting to the changing neural demands [Bassett et al., 2006].

Up to date, the study of functional brain networks is based in a common methodology (regardless of the modality of recording activity). Net topologies are analyzed by means of relation matrices in which two different nodes (electrode, voxel, source region) are supposed to be linked if some defined relation exceed a positive threshold. Then, the topology of the network is analyzed in the context of graph theory.

Although this methodology has offered very interesting insights into global and integrative aspects of brain function [Sporns et. al., 2004], human cognition is associated with rapidly changing and widely distributed neural activation patterns. The brain constitutes a paradigmatic example of a dynamical system in which the relations between regions, even in rest state, create and transform complex functional networks. Evidence suggests that the emergence of unified neural processes is mediated by the continuous formation and destruction of functional links over multiple time scales [Varela et al., 2001], but only static networks have been defined over long periods, neglecting possible instantaneous time–varying properties of the topologies. Simulations on a network with nonlinear neuronal dynamics have shown that functional networks recovered from long windows of neural activity (minutes) largely overlap with the underlying structural network, while networks recovered from consecutive shorter time windows (seconds) present significant fluctuations in their functional topology [Honey et. al., 2004].

Here we propose to study how the topologies of the brain networks are modified by an external event; in the same way that scalp potentials vary across time and frequency, it is evident that the underlying networks should adapt and modify their topologies to satisfy the requirements imposed by the processing of the stimuli. The idea that perception and cognition depend critically on patterns of synchronization and desynchronization that create and destroy –in time– functional networks, calls for a time–varying analysis of the topological reconfigurations underwent by the brain networks. To do that, we present a new methodology that allows characterizing the dynamic evolution of functional brain networks on the time-frequency space: the *Event-Related Networks (ERNs).*

2. Material and Methods

The proposed approach is depicted in Fig. 1. By using any of the available methods used to define relations between different brain regions (wavelet coherence, AR-based measures, etc), it is possible to obtain an event-related relation matrix at each point of the time–frequency space. Then, a statistical criterion is used to assess the statistical significance of the functional connections. These relation matrices house (at each time–frequency point) the topologies of the functional nets associated with the ongoing brain processes elicited by the event. Once that these matrices are obtained the parameters of the functional network can be estimated. Then, a time–frequency varying characterization of the network topology is achieved. Finally, to assess the SW behavior, the topological features of the real brain networks are compared with equivalent regular and random networks.

To illustrate our approach, we have analyzed the responses recorded during the visual presentation of non-familiar pictures. The event-related brain responses to 48 images were recorded with a whole-head MEG system over three epileptic patients, digitized at 1.25 kHz and filtered at 0-200 Hz. Images were presented for 150 ms with an inter-stimulus interval of 2 s.

To assess the functional connection, we computed the phase locking value (PLV) between all pairs of sensors [Varela et al., 2001]. The PLV between any pair of sensors is inversely related to the variability of phase differences across trials. If the phase difference varies little across trials, the distribution of the phase difference is concentrated around a preferred value, and PLV < 1. In contrast, under the null hypothesis of a uniformity of phase distribution, PLV values are close to zero. Finally, to assess whether two different sensors are functionally connected, we calculated the significance probability of the PLV values by a Rayleigh test of uniformity of phase [Fisher 1989]. In our study, the threshold of significance was set at $p = 0.01$.

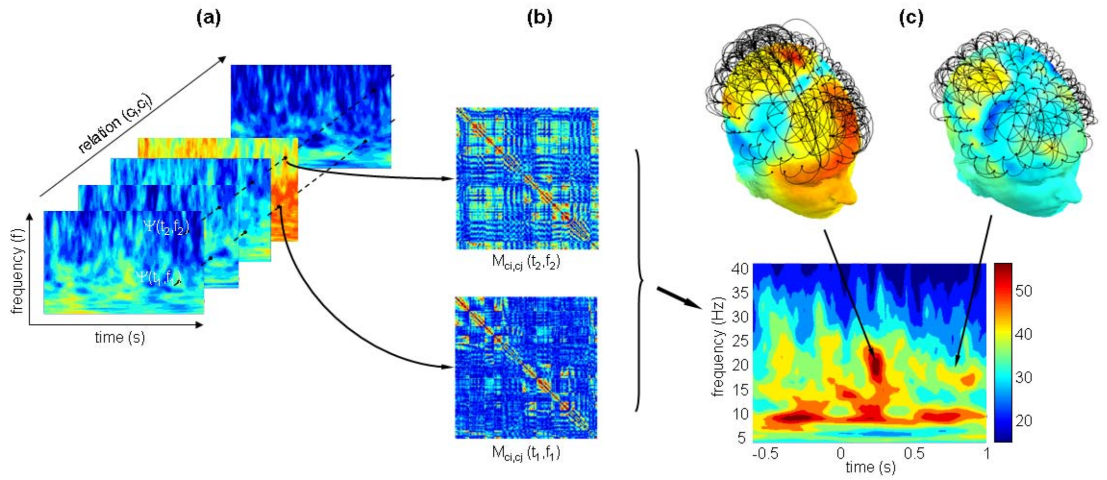


Figure 1. *Extraction of the event related brain networks: (a) from time-frequency relations between all pairs of signals,(b) the functional connectivity matrices are extracted for each time-frequency point and then, (c) a representation of the topological parameters in the time-frequency space is extracted.*

Once the interaction matrices are determined, the topological properties of the related networks can be studied [Boccaletti et al., 2006]. Here we use three key parameters: mean degree K, clustering index C and efficiency E. They allowed us to characterize the network topology and its evolution. The degree of a node k_i represents the number of connections of this node. By averaging across all nodes, K, is obtained. The clustering index quantifies the local density of connections in a node's neighborhood. The clustering coefficient of a node c_i is calculated as the number of links between the node's neighbors divided by all their possible connections while C is defined as the average of c_i taken over all nodes of the network [Watts et al., 1998]. The efficiency E provides a measure of the network's capability for parallel information transfer between nodes. It is defined as the inverse of the harmonic mean of the shortest path length L_{ij} between each pair of nodes *ij* [Latora et al., 2001]. For each node, the E_i is defined as the inverse of the harmonic mean of the minimum path length between the node *i* and all other nodes in the network.

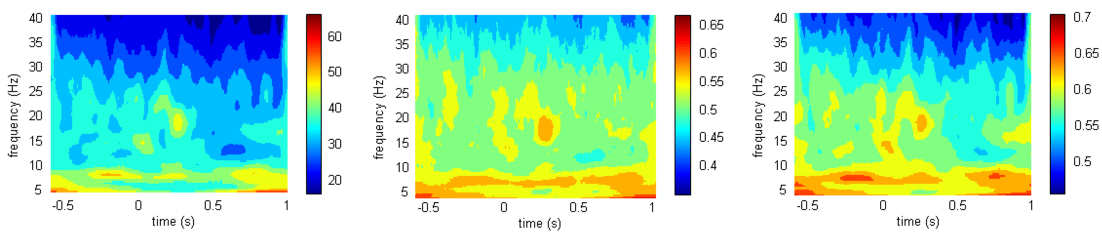
To assess small–world properties, the characteristic mean cluster index and global efficiency coefficients were compared with those obtained from equivalent regular and random networks. Regular networks were obtained by rewiring the links of each node to its nearest (in the sensors space) neighbors, yielding nearest-neighbor connectivity with the same degree distribution as the original network. To create an ensemble of equivalent random networks we rewired each edge of the original network randomly, avoiding self and duplicate connections. As a result, the obtained randomized network preserve the same mean degree as the original network, while the rest of the wiring structure is random. Typically, a small–world network present a greater E_{sw}, than a regular lattice, but less than random networks, $E_{lat} < E_{sw} < E_{rand}$; while for the mean cluster index, $C_{rand} < C_{sw} < C_{lat}$ is expected [Watts et al., 1998].

In the practical experiment, we have calculated the topological parameters of the functional networks elicited by -unexpected- images. The mean degree, clustering index and efficiency were calculated at each point of the time-frequency space between 600 ms before and 1 s after the onset of the stimulus, covering the 3 to 43 Hz frequency range. Although topological features can also be straightforwardly generalized to weighted networks, here we defined the functional connections as undirected and unweighted links between sensors. To further illustrate the evolution of functional brain networks, we also obtained and analyzed the topographical distribution of the local parameters. In that sense, we calculated the local k_i , c_i and E_i, for each sensor of the network and studied their distribution over the scalp.

3. Results

Our most important finding here is that functional connectivity patterns are not time-invariant, but instead they exhibit a rich time-frequency structure. All the topological features present highly varying time-frequency evolutions during the stimulus processing. More specifically, a series of synchronization/desynchronization patterns follow the stimulus presentation evidencing a continuous time-frequency dependent reconfiguration of the functional brain networks (see Fig. 2).

Whereas functional networks in frequency bands over 30 Hz do not show remarkable variations, the most pronounced changes in the SW features seem to be constrained to a frequency band between 5 and 30 Hz. All the parameters exhibited high values in a frequency band close to 10 Hz, a spectral component mostly involved in the processing of visual information. The presentation of the stimulus is accompanied by a sudden change in the connectivity, and a highly connected pattern is induced at about 250 ms, in the 15 to 25 Hz band, suggesting a connectivity induced by the unexpected sensory stimuli. This is followed by large patterns of variation in the topological parameters that indicates a rapid reconfiguration of the functional networks likely related to the stimulus processing.



(a) (b) (c)

Figure 2. *Time-frequency representation of topological features extracted from functional brain networks associated to a visual stimulus presentation (arriving at t=0). (a) Mean degree, (b) clustering index, (c) efficiency. The represented values correspond to the average over three subjects.*

The analysis of the local parameters also showed time-frequency varying distributions over the scalp. In Fig. 3, we have depicted the evolution of the local degree and network configuration for three different time instants (250 ms before and 250 and 750 ms after the presentation of the stimulus) and two selected frequencies (10 Hz and 18.5 Hz). Both, network indices and the topographical distribution of the local parameters over the scalp vary across time and frequency. It should be noted that, for the same time instant, the networks at different frequencies behave differently. 250 ms before the stimulus arrival, the network present a highly connected area in the parietal region at frequencies around 10 Hz, while for 18.5 Hz two regions (frontal and one more occipital) can be observed. After the stimulus arrival, the highly connected pattern of synchronization elicited at t ~ 250 ms for frequencies in the beta range is characterized by two clusters that are interconnected by long-range connections, marking a coordination between the two distant regions. After that, the processing of the stimulus reshapes completely the configuration of the local parameters; for the 18.5 Hz representation, the local degree decreases and the long-range connections disappear. For activities at 10 Hz topography, the frontal "activation" remains, while the parietal one disappears and new long-range connections are established from frontal to more occipital areas.

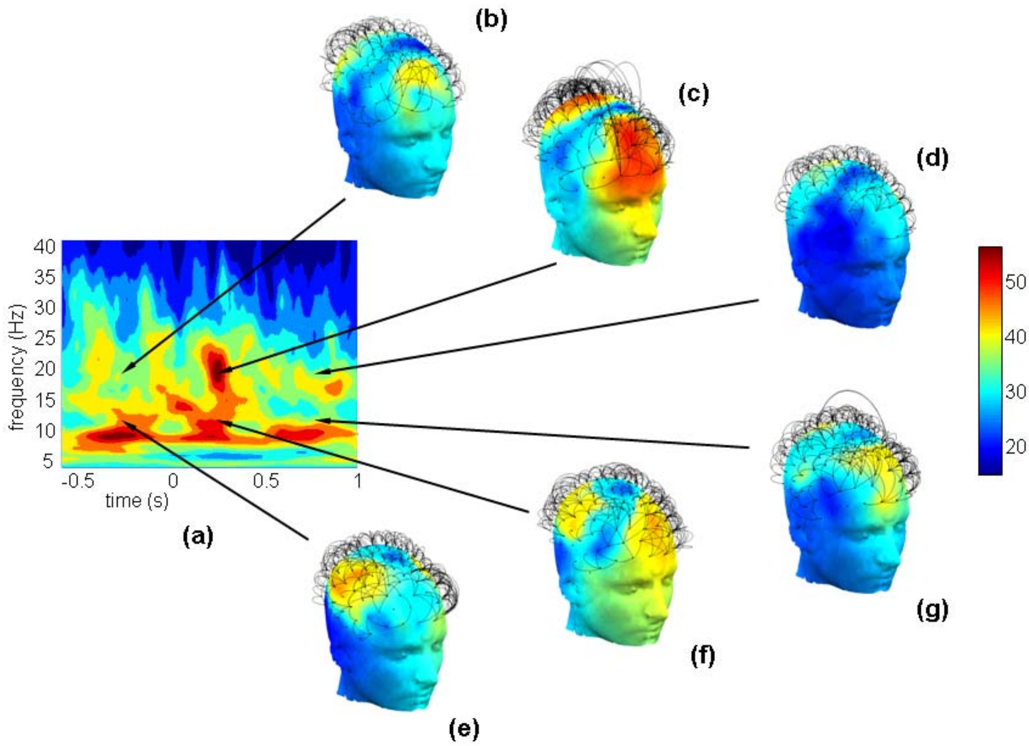


__Figure 3.__ Configurations of the time-frequency dependent functional networks. (a) Evolution of the mean degree for the first subject analyzed. As in the Fig 2, the stimulus is presented at t = 0 s. (b) Combined representation of the topographic distribution of the local degree parameter for time instant t = -0.25 ms, frequency f =18.5 Hz. (c) Same representation as (b) for t = 0.25 ms after the presentation of the stimulus, f =18.5 Hz. (d) t =0.75, f =18.5 Hz. (e) t =-0.25, f =10 Hz. (f) t =0.25, f =10 Hz. (g) t =0.75, f =10 Hz. An evident reconfiguration of the networks is observed (Only links with PLV ∈ [0.6, 0.7] are represented)

Compared to random and regular configurations, for all time-frequency points, $C/C_{rnd}>1$, $C/C_{lat}<1$, $E_{lat}/E<1$ and $E_{rnd}/E>1$ (results not shown), indicating that, despite of the topological variability, brain networks maintain a SW architecture.

4. Discussion

In summary, here we have proposed a new methodology to study the time-frequency evolution of the functional brain connectivity that allows an instantaneous description of the brain networks.

Applied over a visual stimulus paradigm, the exposed framework reveals that the functional brain networks present a highly evolving structure, but maintaining a small-world topology all over the time and frequency. This is a remarkable result, insofar as it suggests that the processing of a stimulus involves an optimized (in SW sense) functional integration of brain regions by a dynamic reconfiguration of links. It provides further support to previous works suggesting that functional brain networks are able to manage and integrate local interactions in global processes allowing an efficient transfer of information, but assuring their capability of adaptation to satisfy changing neural demands [Varela et al., 2001].

Variations in the indexes associated to the evolution of the small-world topology could determine different episodes of the brain processing. Moreover, it could allow to detect characteristic patches of time-frequency ranges associated to specific modifications of the small-world topology driven to satisfy the requirements of the demanded task .

On the other hand, the exposed framework offers an *instantaneous* and *global* description of the interrelations established in the brain. Human cognition is the result of dynamical processes unfolded within the networks of the brain, and the study of their evolution could offer new fundamental insights into basic aspects of the brain function.

For the first time we have evaluated the topological properties of the functional brain networks elicited by a stimulus. Empirical evidence suggests that differences in the event related potentials occur between different cognitive states or in some forms of disease. Diseases associated with disruptions in integrative neural communication should present anomalous patterns of evolution between successive topological states; we have used this methodology over MEG recordings, but applied to other functional imaging techniques (EEG and fMRI), the ERNs approach could provide new insights into the dynamics of functional networks involved in pathological and cognitive brain processes.

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