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The functional connectivity of different EEG bands moves towards small-world network organization during sleep

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Abstract

Objective: To analyze the functional connectivity patterns of the different EEG bands during wakefulness and sleep (different sleep stages and cyclic alternating pattern (CAP) conditions), using concepts derived from Graph Theory.
Methods: We evaluated spatial patterns of EEG band synchronization between all possible pairs of electrodes (19) placed over the scalp of 10 sleeping healthy young normal subjects using two graph theoretical measures: the clustering coefficient (Cp) and the characteristic path length (Lp). The measures were obtained during wakefulness and the different sleep stages/CAP conditions from the real EEG connectivity networks and randomized control (surrogate) networks (Cp-s and Lp-s).
Results: We found values of Cp and Lp compatible with a small-world network organization in all sleep stages and for all EEG bands. All bands below 15 Hz showed an increase of these features during sleep (and during CAP-A phases in particular), compared to wakefulness.
Conclusions: The results of this study seem to confirm our initial hypothesis that during sleep there exists a clear trend for the functional connectivity of the EEG to move forward to an organization more similar to that of a small-world network, at least for the frequency bands lower than 15 Hz.
Significance: Sleep network "reconfiguration" might be one of the key mechanisms for the understanding of the "global" and "local" neural plasticity taking place during sleep.

Keywords: Sleep; Small-world networks; Graph analysis; Functional connectivity; Cyclic alternating pattern; EEG bands; Human

1. Introduction

We have recently reported that the network organization of the EEG slow-wave synchronization during sleep shows features characteristic of small-world networks (Ferri et al., 2007), and that this type of organization is slightly but significantly more evident during the sleep cyclic alternating pattern (CAP) (Terzano et al., 1985, 2001) A1 subtypes (Appendix A contains details on CAP analysis and functional meaning). These results show that using graph theoretical measures to characterize the complexity of functional brain networks during sleep is useful and seems to support the idea that sleep is a period during which slow-wave synchronization shows optimal network organization for information processing. There is increasing evidence that neural networks with synaptic plasticity, if "left on their own", will automatically move toward a more optimal state; such a process might be involved during development, but also – on shorter time scales – during sleep (Kwok et al., 2007; Siri et al., 2007; van den Berg and van Leeuwen, 2004).

A graph is a basic representation of a network, which is essentially reduced to nodes (vertices) and connections

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(edges); in our case each recording electrode can be seen as a node and significant correlations between EEG signals as edges. Graphs are characterized by a clustering coefficient (Cp) and a characteristic path length (Lp), among other measures. Cp is a measure of the local interconnectedness of the graph, whereas Lp is an indicator of its overall connectedness (Boccaletti et al., 2006). Appendix B reports the mathematical details of the graph theoretical analysis used in this study. Watts and Strogatz (1998) have shown that graphs with many local connections and a few random long distance connections are characterized by a high clustering coefficient (like ordered networks) and a short path length (like random networks); such near-optimal networks, which are intermediate between ordered and random networks, are designated as "small-world" networks. Since then, many types of real networks have been shown to have small-world features (Amaral and Ottino, 2004; Strogatz, 2001). Patterns of anatomical connectivity in neuronal networks are particularly characterized by a high clustering and a small path length (Watts and Strogatz, 1998); moreover, these tools have been successfully applied to the analysis of awake multichannel EEG and MEG recordings in different studies in normal and pathological conditions (Bartolomei et al., 2006; Micheloyannis et al., 2006a,b; Reijneveld et al., 2007; Stam, 2004; Stam et al., 2007).

The aim of this new study was to analyze the EEG spatial connectivity patterns at different frequency bands, including the already studied slow-wave activity, based on the hypothesis that they are all probably characterized by a complex spatial connectivity pattern, and to observe eventual differences between them. The hypothesis is that sleep is a complex and active recovery process wherein brain networks move toward a more small-world network state, compared to the wake state before the onset of sleep. For this reason, we utilized the tools of the graph theory which are able to characterize complex networks (Amaral and Ottino, 2004; Sporns et al., 2004; Strogatz, 2001) and analyzed wakefulness and the different sleep stages, as well as CAP and non-CAP (NCAP) conditions.

2. Subjects and methods

2.1. Subjects and polysomnographic recording

Ten healthy subjects (7 females and 3 males, aged 25–35 years) were included in this study. They all had a regular life routine, did not smoke and did not take any alcohol drink in the 3 days preceding the study. These subjects are the same we analyzed in our previous study (Ferri et al., 2007).

All subjects underwent one overnight polysomnographic recording, after one adaptation night, which comprised EOG (2 channels), EEG (19 channels, Ag/AgCl electrodes placed according to the 10–20 International System referred to linked-ear lobes: Fp2, F4, C4, P4, O2, F8, T4, T6, Fz, Cz, Pz, Fp1, F3, C3, P3, O1, F7, T3, T5), EMG of the submentalis muscle and ECG. Recordings were carried out using a Brain Quick Micromed System 98 recording machine and signals were sampled at 256 Hz and stored on hard disk for further analysis. EEG signals, in particular, were digitally band-pass filtered at 0.1–120 Hz, 12-bit A/D precision. All subjects gave their informed consent for the procedures and the Local Ethical Committee approved the study.

2.2. Sleep scoring

Sleep stages were scored following standard criteria (Rechtschaffen and Kales, 1968) on 30-s epochs. Subsequently, each CAP-A phase was detected in each recording (on the C3/A2 or C4/A1 derivation), during NREM sleep, and classified into three subtypes (A1, A2, and A3), according to the rules defined by Terzano et al. (2001). CAP-A phases were manually marked on screen by means of the sleep analysis software Hypnolab 1.2 (SWS Soft, Italy). This process allowed us to obtain a complete characterization of the sleep macrostructure (stages) and microstructure (CAP).

2.3. Graph theoretical analysis

Functional connectivity was determined by computing the synchronization likelihood between all pair wise combinations of channels, resulting in a 19 by 19 connectivity matrix; synchronization likelihood analysis of a very similar data set was reported in some of our previous papers (Ferri et al., 2005b, 2006). The synchronization likelihood is a general measure of the dynamical (linear and nonlinear) interdependencies between a time series (EEG channel) and one or more other time series (Stam and van Dijk, 2002). Briefly, from two discrete time series x_i and y_i vectors are reconstructed with the method of time-delay embedding. The synchronization likelihood at time i is then defined as the likelihood (between 0 and 1), averaged over all j, that the distance between Y_i and Y_j is smaller than a cutoff distance r_{cutoff}, given the distance between X_i and X_j is smaller than r_{cutoff}. Synchronization likelihood close to 0 indicates no coupling, whereas a synchronization likelihood = 1 indicates complete coupling (for a complete mathematical description of the computation of SL refer to Appendix C). For the computation of SL, an average reference montage was used in order to minimize artifactual sources of synchronization; SL is highest for the linked-ears montage, and substantially lower for the other types of montages (Stam and de Bruin, 2004). The linked-ears montage accentuates long-distance coupling at the cost of a small-scale detail; the average montage has intermediate properties and was used in this study (Nunez et al., 1997; Stam and de Bruin, 2004). The parameters used in this study for the computation of the synchronization likelihood were the same as those utilized in our previous studies on similar data sets (Ferri et al., 2005b, 2006, 2007), following the method described by Montez et al. (2006) to choose the parameters.