Unconsciousness reconfigures modular brain network dynamics

S. M. del Pozo[1,2], H. Laufs[3], V. Bonhomme[4,5,6], S. Laureys[6], P. Balenzuela[1,2], and E. Tagliazucchi[1,2]

[1]Departamento de Física, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires. Buenos Aires, Argentina.

[2]Instituto de Física de Buenos Aires (IFIBA), CONICET. Buenos Aires, Argentina.

[3]Department of Neurology, Christian Albrechts University, Kiel, Germany

[4]Anesthesia and Intensive Care Laboratory, GIGA-Consciousness, GIGA Institute, University of Liège, Liège, Belgium

[5]University Department of Anesthesia and Intensive Care Medicine, Centre Hospitalier Régional de la Citadelle, Liège, Belgium

[6]Department of Anesthesia and Intensive Care Medicine, CHU Liège, Liège, Belgium

[7]Coma Science Group, GIGA Consciousness, University of Liège, Liège,Belgium

Abstract

In this work we used complex network theory to study the dynamics of time-dependent functional brain networks obtained from functional magnetic resonance imaging (fMRI) data during conscious wakefulness and states of reduced consciousness. In order to detect heterogeneous temporal networks communities, we developed a new benchmark to set the optimal parameters of a multilayer modularity maximization algorithm. Then we measured the size and flexibility of the largest multilayer module. We found that unconsciousness reconfigured network flexibility and reduced the size of the largest spatiotemporal module, which we identified with the dynamic core. Our results represent a first characterization of modular brain network dynamics during states of unconsciousness measured with fMRI, adding support to the dynamic core hypothesis of human consciousness.

Keywords: multilayer networks, community detection, fMRI, sleep, consciousness.

Introduction

One of the most influential hypothesis concerning the relationship between conscious experience and neural processes in the human brain is Edelman and Tononi's dynamic core hypothesis [2]. According to this hypothesis, consciousness must be understood as a process that unfolds over time (the "dynamic core") comprising an ever-changing network of regions that exchange information over relatively short time spans. The dynamic core should present a very large number of possible configurations, corresponding to the multitude of available conscious experiences. However, these configurations must also be constrained to represent highly integrated brain states, so the dynamic core consists of a sequence exploring an ample repertoire of highly integrated brain states.

The theory of complex networks provides a framework to directly evaluate the presence of integration and segregation in neuroimaging data acquired during different states of consciousness [3]. A sequence of brain states can be represented as a multilayer network, with each layer encoding transient functional interactions between brain regions during a given time period [4], and the dynamic core can be represented as a time-dependent module evolving in this network. Over the last years, modularity maximization algorithms have been applied to multilayer networks to reveal the rapid and transient structure of whole-brain dynamic networks. However, the relationship between consciousness and the modular structure of multilayer brain networks remains to be investigated.

To clarify this relationship, we constructed multilayer connectivity networks from functional magnetic resonance imaging (fMRI) recordings acquired during the different stages of human non-rapid eye movement (NREM) sleep, and under the effect of propofol, a general anesthetic which increases inhibitory neurotransmission. Our main purpose was to obtain the time-dependent modular structure of these networks using the multilayer Louvain algorithm [9], a method with several free parameters related to the connectivity strength between temporal layers, and the characteristic size of the detected modules. Previous reports using this algorithm either employed an *ad-hoc* choice of parameter values, or performed an exhaustive exploration of parameter space [4, 6]. We introduced a new benchmark for the detection of modules in time-dependent networks with scale-free degree and module size distributions, adapted from a benchmark developed for static networks [5].

After parameter selection using this method, we applied the multilayer Louvain algorithm to obtain the time-dependent modular structure of fMRI functional connectivity networks.

Materials & Methods

Module detection in multilayer networks: We applied a generalized multilayer version of the Louvain algorithm to detect and track modules over time (http://netwiki.amath.unc.edu/GenLouvain/GenLouvain).

Benchmark for time-dependent module detection: We first reproduced a benchmark for static complex modular networks introduced by Lancichinetti et al. [5]. Then we created in this benchmark a temporal evolution through two different dynamic processes adapted from Granell et al., 2015 [8]: merge-split and grow-shrink module dynamics. The combination of these two processes allowed us to represent the most frequent behaviours seen in the dynamics of real modular systems. In Figure 1 **A** the rewiring steps used to generate the dynamics of division and contraction of communities are shown, where the colors of the nodes represent their final communities. Further details can be found in [1].

Node flexibility and the largest multilayer module: We defined two metrics based on the module membership matrix G_{it} given by the multilayer Louvain algorithm. First, we defined the flexibility of a node within a certain multilayer module M, F_i, as the normalized number of times that node entered or left M:

$$F_i = \frac{|\{t : M_{it} \neq M_{it+1}\}|}{T} \tag{1}$$

where M_{it} indicates whether node i at time t belongs to module M, and T is the total number time steps. We computed F_i for the largest multilayer module. We also defined the size of this module (LMM) as the normalized size of the largest module in G_{it},

$$LMM = \frac{\max_i |G_{it}|}{NT} \tag{2}$$

where N is the number of nodes and T the total number of volumes in the recording, so NT is the maximum possible size for the largest module.

More information related to the fMRI data sets, the construction of dynamic networks from fMRI data and statistical analyses are available in [1].

Results

Time-dependent benchmark and parameter selection: We investigated the performance of the multilayer Louvain algorithm [9] based on introducing equally weighted (ω) connections between consecutive temporal layers and equal resolution parameters across layers (γ). Thus, the module detection algorithm depended only on these two parameters. In Figure 1 **B** we introduced a grid of γ and ω values, and for each pair of values we measured the Rand index between heuristic approximations to the ground-truth modules and those detected using the multilayer Louvain algorithm, averaging the results over 500 independent realizations.

The optimal parameters obtained following this procedure were $\gamma = 0.55$ and $\omega = 1$ for both benchmarks (values are indicated as black boxes in Figure 1 **B**). Then, in Figure 1 **C** it is shown the modular structure detected by the multilayer Louvain algorithm using the optimal parameters for merge and split processes. The red lines indicate the expected distribution of module membership labels.

Modular structure of dynamic brain connectivity networks: We applied the multilayer Louvain algorithm using the optimal parameters inferred from the benchmarks to dynamic functional connectivity networks obtained from fMRI data. We computed and compared the flexibility of nodes within the largest multilayer module between wakefulness and each sleep stag. We observed that the majority of nodes decreased their flexibility during sleep, and that regions presenting decreased flexibility during sleep were related to sensory perception, and also included subcortical regions that serve as intermediate stages for the propagation of sensory information towards the cortex, such as the thalamus. We also performed the same analysis and statistical comparison for wakefulness vs. propofol sedation and anesthesia, without finding significant results. Further details can be found in [1].

Finally, we compared the regional probability of belonging to the largest multilayer module in wakefulness vs. sleep, and propofol-induced sedation (S) and loss of consciousness (LOC). Only statistical comparisons between wakefulness, N3 and LOC yielded significant results. Figure 1 **D** presents a comparison of these changes. While changes were more widespread and significant during N3 sleep, LOC was also associated with decreases in sensorimotor regions, and increases in frontal regions.

In Figure 1 **E**, a scatter plot of the change in the probability of belonging to the largest multilayer module for LOC vs. N3 shows that even though less regions were significant for LOC, the pattern of changes was similar to that measured during N3 sleep (R=0.39, p<0.00001). Also, both N3 (0.411±0.011; mean±standard error) and LOC (0.347±0.013) were characterized by smaller sizes of their largest multilayer modules relative to wakefulness (0.446±0.005 and 0.397±0.009 for the sleep and propofol baseline, respectively), as shown in Figure 1 **F**.

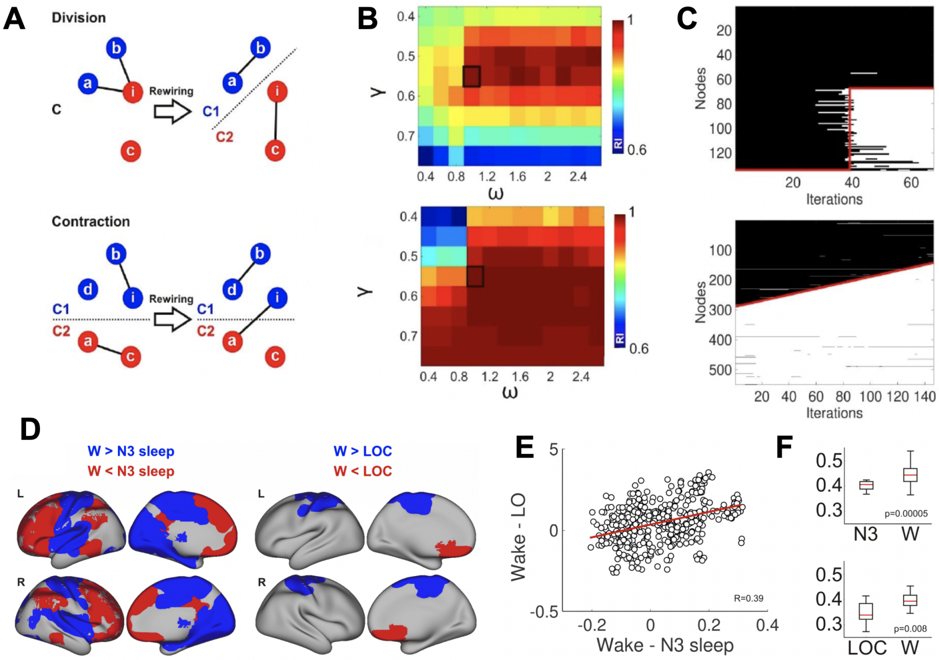

Figure 1: *[**A-C**] Benchmark for time-dependent heterogeneous networks based constructed from two dynamic processes (division and contraction). [**D-F**] Application of the optimized algorithm on data sets.*

Discussion

We investigated for the first time modular brain network dynamics during states of unconsciousness, finding converging evidence of a reconfiguration of the largest multilayer module during deep sleep and general anesthesia. We interpreted these changes in the light of the dynamic core theory, concluding that unconsciousness results in its fragmentation in spite of preserved stability. Future studies should assess whole-brain dynamics simultaneously with different methods to understand whether the dynamic core fluctuates over scales inaccessible to fMRI, and whether these fluctuations are manifest at the behavioral and cognitive levels.

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