



## Modular structure of functional networks in olfactory memory



David Meunier<sup>a,\*</sup>, Pierre Fonlupt<sup>b</sup>, Anne-Lise Saive<sup>a</sup>, Jane Plailly<sup>a</sup>, Nadine Ravel<sup>a</sup>, Jean-Pierre Royet<sup>a,\*</sup>

<sup>a</sup> *Olfaction: from coding to memory team, INSERM U1028, CNRS UMR 5292 – Université Lyon 1, Lyon F-69366, France*

<sup>b</sup> *Brain, Dynamics and Cognition team, INSERM U1028, CNRS UMR 5292 – Université Lyon 1, Bron F-69675, France*

### ARTICLE INFO

#### Article history:

Accepted 15 March 2014

Available online 22 March 2014

#### Keywords:

Graph theory  
Functional connectivity  
Neural network  
Modularity  
Olfactory memory  
Signal detection theory

### ABSTRACT

Graph theory enables the study of systems by describing those systems as a set of nodes and edges. Graph theory has been widely applied to characterize the overall structure of data sets in the social, technological, and biological sciences, including neuroscience. Modular structure decomposition enables the definition of sub-networks whose components are gathered in the same module and work together closely, while working weakly with components from other modules. This processing is of interest for studying memory, a cognitive process that is widely distributed. We propose a new method to identify modular structure in task-related functional magnetic resonance imaging (fMRI) networks. The modular structure was obtained directly from correlation coefficients and thus retained information about both signs and weights. The method was applied to functional data acquired during a yes–no odor recognition memory task performed by young and elderly adults. Four response categories were explored: correct (Hit) and incorrect (False alarm, FA) recognition and correct and incorrect rejection. We extracted time series data for 36 areas as a function of response categories and age groups and calculated condition-based weighted correlation matrices. Overall, condition-based modular partitions were more homogeneous in young than elderly subjects. Using partition similarity-based statistics and a posteriori statistical analyses, we demonstrated that several areas, including the hippocampus, caudate nucleus, and anterior cingulate gyrus, belonged to the same module more frequently during Hit than during all other conditions. Modularity values were negatively correlated with memory scores in the Hit condition and positively correlated with bias scores (liberal/conservative attitude) in the Hit and FA conditions. We further demonstrated that the proportion of positive and negative links between areas of different modules (i.e., the proportion of correlated and anti-correlated areas) accounted for most of the observed differences in signed modularity. Taken together, our results provided some evidence that the neural networks involved in odor recognition memory are organized into modules and that these modular partitions are linked to behavioral performance and individual strategies.

© 2014 Elsevier Inc. All rights reserved.

### Introduction

Most cerebral imaging functional studies have used univariate statistical analyses to localize brain regions involved in specific cognitive operations (Rissman et al., 2004). However, the concept of the brain as a large complex network of interconnected elements has become dominant in modern neuroscience (Mesulam, 1990; Varela et al., 2001). Understanding how brain regions specifically communicate with one another during a particular cognitive task remains challenging.

The term “brain connectivity” is used at the functional level to describe the organization, interrelationships, and integrated performance of different brain regions (Horwitz, 2003). A distinction is made between methods that consider correlation or covariance between signals

in different regions (functional connectivity) and methods that attempt to describe or make inferences about the direction of influence between regions (effective connectivity) (Friston, 1994; Rogers et al., 2007). Techniques for measuring functional connectivity during tasks include correlations between standardized regression coefficients (Rissman et al., 2004), principal and independent component analysis (PCA and ICA) (Calhoun et al., 2001; McKeown and Sejnowski, 1998), and graph theoretical methods (Bullmore and Sporns, 2009; Fornito et al., 2013). Techniques that measure effective connectivity include psychophysiological interaction (PPI) (Friston et al., 1997), structural equation modeling (SEM) (McIntosh and Gonzalez-Lima, 1994), Granger causal mapping (Roebroeck et al., 2011), and dynamic causal modeling (DCM) (Friston et al., 2003; Penny et al., 2004).

While several studies have explored the functional connectivity of the olfactory network in animals (e.g., Spors et al., 2012; Wilson and Yan, 2010; Wilson et al., 2011), very few human cerebral imaging studies have been performed, and most have used effective connectivity. Zald et al. (1998) used covariance matrices based on PET data to elucidate the functional connectivity between the amygdala and the

\* Corresponding authors at: Olfaction: from coding to memory team, INSERM U1028, CNRS UMR 5292 50, Avenue Tony Garnier, Université Lyon 1, Lyon F-69366, France. Fax: +33 4 37 28 76 01.

E-mail addresses: [David.Meunier@olfac.univ-lyon1.fr](mailto:David.Meunier@olfac.univ-lyon1.fr) (D. Meunier), [royet@olfac.univ-lyon1.fr](mailto:royet@olfac.univ-lyon1.fr) (J.-P. Royet).

orbitofrontal cortex (OFC) during emotional olfactory tasks. Plailly et al. (2008) combined functional magnetic resonance imaging (fMRI) with DCM to measure attention-dependent network coherence within olfactory pathways. Haase et al. (2011) used SEM to test a functional connectivity model during recognition memory in individuals genetically at risk for Alzheimer's disease. Karunanayaka et al. (2013) used whole-brain ICA decomposition to identify subcomponents involved in olfactory perception as well as SEM to study the directionality of interactions between these subcomponents. PPI analyses have also been used to demonstrate amplified functional connectivity between several olfactory-related regions, either in response to negative odors, particularly in anxiety (Krusemark and Li, 2012), or during passive smelling (Nigri et al., 2013).

We recently investigated the neural basis of odor recognition in young and elderly adults (Royet et al., 2011) by exploring correct (Hit) and incorrect (false alarms, FA) recognition and correct (CR) and incorrect (Miss) rejection. To characterize the brain responses in terms of functionally connected systems, we examined the functional relationships between the main regional foci using multivariate analyses of covariance and canonical variate analyses. We observed that significant activity in the hippocampus and parahippocampal gyrus was associated with correct recognition of odors. In this study, we go a step further by incorporating graph theory to study the differences between the networks underpinning correct and incorrect olfactory memories and to demonstrate how the brain areas composing these networks interact with each other.

Graph theory is used to quantify the overall properties of any system that can be described as a graph, i.e., a set of nodes and a set of edges representing interactions between nodes. Graph theory has been widely applied to research fields as varied as biology, sociology, and technology science (Barabási, 2003; Newman et al., 2006) and, more recently, to brain data (Bullmore and Sporns, 2009). Graph theory has been used in fMRI to analyze both resting-state functional data (e.g., Achard and Bullmore, 2007; Achard et al., 2006) and task-related data (Bassett et al., 2011; Ginestet and Simmons, 2011; Park et al., 2012; Shinkareva et al., 2008; Wang et al., 2010).

Among several analyses derived from graph theory, modular decomposition aims at partitioning a network into several modules (also referred to as communities or clusters). Modules are characterized by nodes that work tightly together and less tightly with nodes belonging to other modules (Newman and Girvan, 2004). Modular decomposition is achieved by maximizing a quality function, called modularity, and by assessing how well the nodes fit to modules of a given partition of the network. Modular decomposition has previously been applied to resting-state fMRI (Chen et al., 2008; Fair et al., 2009; Meunier et al., 2009a; Power et al., 2012; Stevens et al., 2012).

Several limitations of modular analysis can result in a loss of information. First, computing modularity over a range of thresholds may lead to issues concerning the independence of the considered samples (Langer et al., 2013). Second, modular analysis considers only positive correlations, which is inadequate for functional connectivity analysis because anti-correlated sub-systems can work in opposition to each other (Fox et al., 2005). Third, statistical comparisons of graphs obtained from different experimental conditions are not straightforward, although some methods have been proposed to compare modular structures between two groups of subjects when data were acquired in the resting-state (Alexander-Bloch et al., 2012; Moussa et al., 2012).

In this article, we investigated the functional networks involved in olfactory recognition memory. We overcame the limitations previously described by using modularity quality functions for weighted and signed graphs (Gómez et al., 2009; Traag and Bruggeman, 2009). We developed statistical validation methods using similarity-based tests to assess the significance of differences obtained at the modular level between the young and elderly adults and between the four memory response categories (Hit, FA, CR, and Miss). We further correlated the modularity values with the behavioral performance of the subjects.

## Materials and methods

The methodology was reported in detail previously (Royet et al., 2011) and is briefly described here. Only the distinct aspects are extensively described in the present study.

### Experimental task and behavioral analysis

#### Subjects

A total of 16 young [7 men; age:  $27.14 \pm 5.27$  years (mean  $\pm$  SD); range: 21.90–37.30] and 22 elderly (11 men; age  $68.64 \pm 3.29$  years; range: 65.00–74.76) right-handed subjects participated in the study. This experiment was conducted in accordance with the Declaration of Helsinki. All subjects provided written informed consent as required by the local Institutional Review Board according to French regulations on biomedical experiments with healthy volunteers [Ethical Committee of CPP-Sud Est II (n CPP A 06-024), DGS2006-0226, May 11, 2006].

#### Stimuli and experiment

The subjects participated in a classical olfactory memory recognition task initially proposed by Engen and Ross (1973). A total of 100 odorants were used, comprising 50 target (old) and 50 distractor (new) odorants. Stimuli were counterbalanced by quality and mean scores of intensity, hedonicity, and familiarity obtained from previous data (Royet et al., 1999). The odorants were presented using an airflow olfactometer, which allowed the stimuli to be synchronized with breathing (Vigouroux et al., 2005). Odorants were delivered through a standard oxygen mask positioned on the subject's face.

Two functional runs corresponding to encoding and retrieval sessions were performed, separated by the structural image acquisition sequence. The 50 target odorants were presented in the encoding session and then interleaved with the 50 distractor odorants in the retrieval session. Odorants were delivered according to an event-related fMRI design with a jittered interstimulus interval of  $\sim 15$  s, depending on the participant's respiration. The order of presentation of the odorants was randomized between participants for both sessions. During the encoding session, participants indicated when they detected an odorant by pressing one button with their right hand. Participants were not instructed about the objective of the next session. During the retrieval session, the participants indicated whether or not they had already smelled the odorant in the first session.

#### Behavioral data analysis

Recognition memory performance was assessed using parameters issued from signal detection theory (Lockhart and Murdock, 1970). Hit, Miss, CR, and FA response categories were assigned based on the experimental conditions (old or new odorants) and the subjects' behavioral answers (yes or no). Two parameters were calculated from the Hit and FA scores: a memory score ( $d'_L$ ) and a response bias score ( $C_L$ ). Corwin (1989) previously described these calculations as follows:

$$d'_L = \ln \frac{HR(1-FR)}{FR(1-HR)} \quad (1)$$

$$C_L = 0.5 \times \ln \frac{(1-FR)(1-HR)}{(HR \times FR)} \quad (2)$$

where  $HR$  represents the Hit rate  $[(N_{Hit} + 0.5) / (N_1 + 1)]$ ,  $FR$  represents the false-alarm rate  $[(N_{FA} + 0.5) / (N_2 + 1)]$ , and  $N_1$  and  $N_2$  represent the number of old and new odorants, respectively, for which the subjects provided an answer. As  $N_1 = N_{Hit} + N_{Miss}$ , and  $N_2 = N_{CR} + N_{FA}$ , information about all 4 response categories are included in both  $d'_L$  and  $C_L$ . The memory scores were good or poor (positive and negative values, respectively). The response bias scores established three individual

Download English Version:

<https://daneshyari.com/en/article/6026861>

Download Persian Version:

<https://daneshyari.com/article/6026861>

[Daneshyari.com](https://daneshyari.com)